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1/77

Request for grant of a patent

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1. Your reference	ARB/BP5730593	
2. Patent application number *(The Patent Office will fill in this part)*	23 DEC 1998	9828565.3
3. Full name, address and postcode of the or of each applicant *(underline all surnames)*	RADEMACHER GROUP ~~LTD.~~ LIMITED ~~THE WINDEYER BUILDING~~ ~~46 CLEVELAND STREET~~ ~~LONDON~~ ~~W1P 6DB~~ BOUVERIE HOUSE 154 FLEET STREET LONDON EC4A 2HX GB	
Patents ADP number *(if you know it)*		7576036001
If the applicant is a corporate body, give the country/state of its incorporation	~~UK~~	
4. Title of the invention	INOSITOL-CONTAINING HEXASACCHARIDES, THEIR SYNTHESIS AND THEIR USES	
5. Name of your agent *(if you have one)*	MEWBURN ELLIS	
"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	YORK HOUSE 23 KINGSWAY LONDON WC2B 6HP	
Patents ADP number *(if you know it)*	109006	

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number	Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application	Number of earlier application	Date of filing *(day / month /year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:* *a) any applicant named in part 3 is not an inventor, or* *b) there is an inventor who is not named as an applicant, or* *c) any named applicant is a corporate body.* *See note (d))*	YES

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Continuation sheets of this form	0
Description	59
Claim(s)	0
Abstract	0
Drawing(s)	8 + 8

10. If you are also filing any of the following, state

Priority documents	0
Translations of priority documents	0
Statement of inventorship and right	0
Request for preliminary examination	0
Request for substantive examination *(Patents Form 10/77)*	0
Any other documents *(Please specify)*	0

11. I/We request the grant of a patent on the basis of this application.

Signature: Mewburn Ellis — Date: 22-12-98

12. Name and daytime telephone number of person to contact in the United Kingdom: ANDREA R. BREWSTER — 0117 926 6411

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Inositol-containing Hexasaccharides, their Synthesis and their Uses

Field of the Invention

The present invention relates to novel inositol-containing hexasaccharides, in particular to hexasaccharides capable of acting as inositol phosphoglycan (IPG) mimetics. It also relates to the synthesis of such hexasaccharides, to intermediate compounds formed during their synthesis, to the uses of the hexasaccharides and to compositions containing them.

Background to the Invention

Many of the actions of growth factors on cells are thought to be mediated by a family of inositol phosphoglycan (IPG) second messengers [1-5]. It is believed that the source of such IPGs is a "free" form of glycosyl phosphatidylinositol (GPI) present in cell membranes. IPGs are thought to be released by the action of phophatidylinositol-specific phospholipases following ligation of growth factor to receptors on the cell surface.

There is evidence that IPGs mediate the action of a large number of growth factors including insulin, nerve

growth factor, hepatocyte growth factor, insulin-like growth factor I (IGF-I), fibroblast growth factor, transforming growth factor β, the action of IL-2 on B-cells and T-cells, ACTH signalling of adrenocortical cells, IgE, FSH and hCG stimulation of granulosa cells, thyrotropin stimulation of thyroid cells and cell proliferation in the early developing ear and rat mammary gland.

The family of IPG second messengers can be divided into two distinct sub-families, A-type and P-type, on the basis of biological activity. The A-type modulate the activity of a number of insulin-dependent metabolic effects such as acetylCoA carboxylase (activates), cAMP dependent protein kinase (inhibits), adenylate cyclase (inhibits) and cAMP phosphodiesterases (stimulates). In contrast, the P-type modulate the activity of enzymes such as pyruvate dehydrogenase phosphatase (stimulates) and glycogen synthase phosphatase (stimulates). The A-type mimic the lipogenic activity of insulin on adipocytes, whereas the P-type mimic the glycogenic activity of insulin on muscle. (See [6 - 9].)

Soluble IPG fractions have been obtained from a variety of animal tissues including rat tissues (liver, kidney, muscle, brain, adipose and heart) and bovine

liver. Until recently, however, it has not been possible to isolate single purified components from tissue-derived IPG fractions, much less in sufficient quantities to allow structural characterisation. Accordingly, prior art studies have been largely based on the biological activities of the fractions, with only speculation, based on indirect evidence from metabolic labelling and cleavage techniques, as to the identity of the active components.

In WO-98/11116 and WO-98/11117 we describe the isolation of active components of A-type and P-type (respectively) IPG fractions from human liver and placental tissue. The biological activity of these isolates is confirmed, and certain aspects of their structure (for instance, mass spectrometry data) and properties are disclosed. A-type substances are defined, for instance, as cyclitol-containing carbohydrates which also contain Zn^{2+} ions and optionally phosphate; P-type substances are said to be cyclitol-containing carbohydrates which also contain Mn^{2+} and/or Zn^{2+} ions and optionally phosphate. The precise chemical structures of the components of the isolated fractions are not, however, disclosed.

Other studies indicate that A-type IPGs are composed

of *myo*-inositol, non-acetylated D-glucosamine, D-galactose and phosphate [6], and P-type of *chiro*-inositol, non-acetylated D-galactosamine, D-mannose and phosphate [7]. We have also obtained, from large quantities of bovine liver, a partially purified glycolipid fraction that after treatment with bacterial phosphatidylinositol specific phospholipase C gave a water soluble fraction that inhibited cAMP dependent protein kinase [10]. This biologically active material could be partially sequenced and the results indicated the presence of a family of substances containing *myo*-inositol, non-acetylated D-glucosamine, an undetermined hexose (either D-mannose or D-galactose), and a terminal *N*-acetyl-D-glucosamine residue. In addition up to four α-D-galactopyranosyl units and up to three phosphate groups seemed to be present [10].

These partial data go some way towards determining the chemical structure of the A-type IPGs, but still leave a considerable number of uncertainties.

Nevertheless, it would be desirable to synthesise IPG analogues with activities at least partially mimicking those of the naturally occurring materials. To this end, we have carried out the synthetic, structural

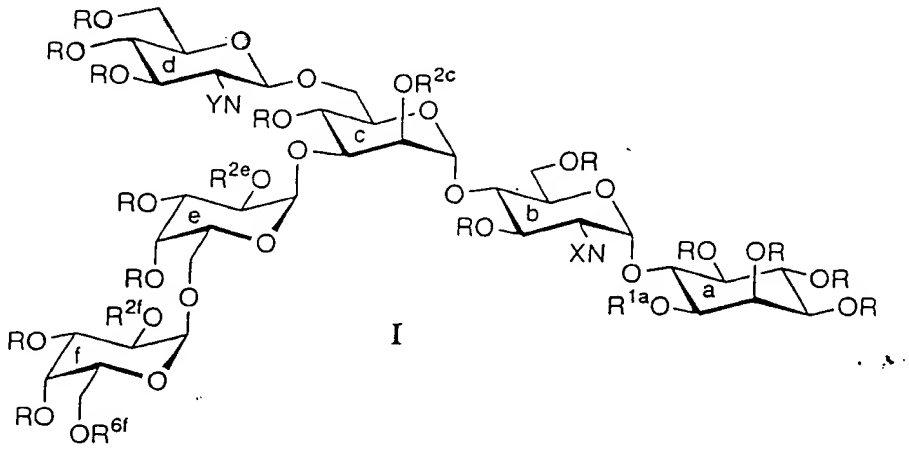
and biological studies documented in [13-17], as a result of which a number of basic sub-structures have been synthesised, their shapes and spectroscopic properties studied and aspects of their potential biological activity investigated. For instance, we have synthesised inositol-containing disaccharides such as those referred to as compounds C3 (1-D-6-*O*-(2-amino-2-deoxy-α-D-glucopyranosyl)-*myo*-inositol 1,2-(cyclic phosphate)) and C4 (1D-6-*O*-(2-amino-2-deoxy-α-D-glucopyranosyl)-*chiro*-inositol 1-phosphate) [14, 15], and demonstrated biological activity, in the form of proliferative effects on the early developing inner ear of a chick embryo, for at least the *myo*-inositol-containing C3 [14].

Frick et al, in *Biochemistry* **1998**, 37, 13421-13436, also disclose the synthesis of IPG analogues, both trisaccharides and hexasaccharides, which include mannose, glucosamine and inositol units. They conclude that a mannose side chain is necessary to maximise the insulin-mimetic activity of their products.

Summary of the Invention

The present invention arises from the design and synthesis of novel hexasaccharides of the general formula

I:



I

wherein:

- each R is independently hydrogen, a phosphate group (PO_3^- or PO_3H for instance) or a protecting group;

- NX represents N_3 or NH_3^+; and

- NY represents a phthalimido group (NPht) or AcHN, with the proviso that the molecule must contain no more than three phosphate groups.

The constituent saccharide units in I are labelled a-f, and in the following description the R groups are referred to according to their positions within each unit, eg, R^{2a} indicates the R group at position 2 in unit a.

Compound I contains the basic saccharide units believed to be present in A-type IPGs, ie, a *myo*-inositol

unit (a), a non-acetylated D-glucosamine unit (b), a mannose unit (c), a terminal *N*-acetyl-D-glucosamine residue (d) and D-galactose units (e) and (f). It also has a reasonable structural overlap with the conserved linear glycan chain of the GPI anchors depicted as formula **2** in Figure 1. Thus, taking into account the immunological evidence that antibody probes generated against **2** cross react with IPGs from rat liver and block some of the effects of insulin [11, 12], compound I can reasonably be expected to be useful as a synthetic analogue, or mimetic, of naturally-occurring A-type IPGs, and hence to have applications in pharmaceutical compositions and methods.

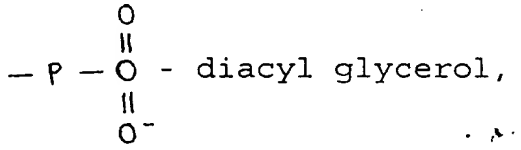
Other aspects of the invention relate to methods for synthesising compounds of formula I and to intermediate compounds generated during the syntheses.

Detailed Description

Compounds of Formula I

The first aspect of the invention provides a compound of formula I, as defined above, or a salt or other derivative thereof. "Derivative" includes coordination complexes, for example with metal ions such

as Zn^{2+}. It also includes so-called "prodrug" forms of the compound, convertible either *in vitro* or *in vivo* into compounds of formula I. An example of a suitable prodrug is a glycolipid derivative in which R^{1a} is:



which may be convertible to I following phospholipase cleavage.

A second aspect of the invention provides a material (whether a compound or composition) which incorporates a compound of formula I, chemically or physically bound to a coupling partner such as a label, a supporting substrate, a carrier, an effector or inhibitor molecule or an immobiliser.

In I, suitable protecting groups for R include menthoxycarbonyl (MntCO), an acetal (in particular, two R groups may together represent a bridging acetal such as *O*-cyclohexylidene, *O*-isopropylidene or *O*-benzylidene), *tert*-butyldimethylsilyl (TBDMS), benzyl (Bn), *tert*-butyldiphenylsilyl (TBDPS), etc... Many protecting groups suitable for use in the syntheses and reactions of saccharides are known and are well documented in standard reference works. The choice depends in part on the route

by which the compound I is synthesised and/or on the uses to which it is to be put, including perhaps on reactions which it is subsequently intended to undergo.

Either or preferably both of R^{1a} and R^{6f} are phosphate. R^{1a} and R^{2a} may together represent a cyclic phosphate group. X is preferably H_3^+. Y is preferably AcH.

Preferred forms of compound I are those which are at least partially deprotected, ie, in which one or more of the R groups is hydrogen. For instance, at least the R groups in units a and b, more preferably units a, b and c, most preferably units a, b, c and d, are either hydrogen or phosphate (eg, R^{1a} is still preferably phosphate).

A particularly preferred form of compound I is that shown as formula **1** in Figure 1, in which all R groups are hydrogen, with the exception of R^{1a} and R^{6f} which are phosphate, X is H_3^+ and Y is AcH.

Preferred protected forms of I are those which have been or could have been prepared by the synthetic methods also provided by this invention (see below). These methods place certain limitations on the nature of the protecting groups R, to ensure the correct stereochemistry of the glycosidic linkages in I, namely:

a) R^{2c}, R^{2e} and R^{2f} are preferably permanent, non-participating protecting groups; and

b) R^{1a} and R^{6f} are preferably temporary protecting groups chosen to permit orthogonal deprotection with respect to all the permanent protecting groups in I.

In addition, NX is preferably a non-participating group, whereas NY is preferably participating.

A participating group is one which participates in a glycosylation reaction and influences the stereochemistry of the glycosidic linkage formed, leading to a 1,2-*trans* linkage. A non-participating group is one which in principle does not influence the stereochemical outcome of a glycosylation reaction.

Preferred protecting groups for I include N_2 for X, Pht for Y and bridging acetals for the pairs R^{2a} and R^{3a}, R^{4a} and R^{5a}, R^{4d} and R^{6d} , R^{3e} and R^{4e} and R^{3f} and R^{4f}.

A particularly preferred protected form of I is that in which R^{1a} is MntCO; R^{2a} and R^{3a} together represent *O*-cyclohexylidene, as do R^{4a} and R^{5a} together; R^{3b}, R^{6b}, R^{2c}, R^{4c}, R^{3d}, R^{2e} and R^{2f} are benzyl (Bn); R^{4d} and R^{6d} together represent *O*-benzylidene; R^{3e} and R^{4e}, and also R^{3f} and R^{4f}, together represent *O*-isopropylidene; and R^{6f} is acetate.

Pharmaceutical Compositions

A third aspect of the invention provides a pharmaceutical composition including a compound, derivative or material according to the first or second aspect, a pharmaceutically acceptable derivative thereof or an antagonist thereto. An "antagonist" to a compound includes a substance having one or more of the following properties:

(a) ability to inhibit release of the compound or its analogue;

(b) ability to reduce the level of the compound via a binding substance (eg, an antibody or specific binding protein); and

(c) ability to reduce the effect(s) of the compound.

An antagonist may be, for example, a specific binding protein or an antibody capable of binding specifically to the compound of interest. It may be a synthetic or naturally occurring substance.

The pharmaceutical composition may include other pharmaceutically acceptable adjuvants such as carriers, buffers, stabilisers or other excipients, depending on the purpose of the composition and its intended route of administration (eg, oral, intravenous or whatever). It

may additionally include other pharmaceutically active ingredients, which may be therapeutically (including prophylactically) active or have some diagnostic function. It may for instance contain insulin, a P-type IPG or IPG analogue, another A-type IPG or analogue, and/or an IPG antagonist. The composition may also, of course, contain more than one compound, derivative or material according to the first or second aspect of the invention.

The composition may be in any suitable form, such as a tablet, capsule, powder or liquid for oral administration, or a solution or suspension for use for instance as a vaccine. Conventional solid or liquid carriers may be used in such formulations. The concentration of the compound, derivative or material contained in the pharmaceutical composition will depend, of course, on the nature and severity of the condition to be treated or diagnosed using the composition, and on the patient to whom and method by which it is to be administered.

Possible uses for the pharmaceutical composition of this third aspect of the invention (which include both therapeutic and diagnostic uses) are described below.

Uses of the Compounds and Compositions

Since compounds of formula I are expected to mimic, at least to an extent, the biological activity of A-type IPGs, they are equally expected to be of use in therapeutic and diagnostic methods based on that activity. Thus, fourth - sixth aspects of the invention provide, respectively, a compound or derivative according to the first aspect, or a material according to the second aspect, or an antagonist thereto, for use in any surgical, therapeutic or diagnostic method; the use of such a compound, derivative, material or antagonist in the manufacture of a medicament for use in any surgical, therapeutic or diagnostic method; and a method of surgery, therapy or diagnosis which involves the use of such a compound, derivative, material or antagonist.

The term "therapy" as used here includes prophylaxis. Moreover, in this section "compound" should be taken to include derivatives, materials and antagonists as referred to in connection with the third aspect of the invention.

The compounds are in particular likely to be of use in treating and/or diagnosing any condition which is related to (ie, which is or can be caused or mediated, directly or indirectly, by, or which is in any way

associated with) insulin activity, in particular the effects of the IPG second messengers. They may be used, for instance, in the treatment and/or diagnosis of disorders in which the lipogenic response of a patient has in some way been affected so that he or she produces a relatively low amount of A-type IPGs in response to growth factors such as insulin.

More particularly, the compounds are likely to be of use in the treatment and/or diagnosis of diabetes, including diabetes due to insulin resistance, insulin resistance in type I diabetes and brittle diabetes, and of conditions associated with insulin resistance or insulin underproduction, such as neurotrophic disorders or polycystic ovary disease.

The use of both P- and A-type IPGs in the diagnosis and treatment of diabetes is disclosed in WO-98/11435. This application discloses that in some forms of diabetes the ratio of P:A-type IPGs is imbalanced and can be corrected by administering a medicament containing an appropriate ratio of P- or A-type IPGs or antagonist(s) thereof. In particular, it describes the treatment of obese type II diabetes (NIDDM) patients with a P-type IPG and/or an A-type IPG antagonist and the treatment of IDDM or lean type II diabetes (body mass index < 27) with a

mixture of P- and A-type IPGs, typically in a P:A ratio of about 6:1 for males and 4:1 for females. The compounds and compositions of the present invention can be employed in such types of treatment.

The compounds of this invention are also likely to be of use in promoting either *in vitro* or *in vivo* neuron proliferation. They may thus have applications in the treatment and/or diagnosis of any condition related to neuron proliferation. The neurons may be central (brain and spinal cord) neurons, peripheral (sympathetic, parasympathetic, sensory and enteric) neurons, or motor neurons. Treatments may involve the treatment of damage to the nervous system, of motor neuron disease, of neurodegenerative disorders or of neuropathy. Damage to the nervous system includes the results of trauma, stroke, surgery, infection (eg, by viral agents), ischemia, metabolic disease, toxic agents, or a combination of these or similar causes. Motor neuron disease includes conditions involving spinal muscular atrophy, paralysis or amyotrophic lateral sclerosis. Neurodegenerative disorders include Parkinson's disease, Alzheimer's disease, epilepsy, multiple sclerosis, Huntingdon's chorea and Meniere's disease:

A therapeutic treatment method in which the

compounds may be used involves the administration to a patient suffering from a relevant condition a therapeutically (which includes prophylactically) effective amount of one of the compounds, preferably in the form of a pharmaceutical composition according to the third aspect of the invention. "Effective amount" means an amount sufficient to cause a benefit (which may be prophylactic) to the subject or at least to cause a change in the subject's condition. The actual amount administered to the patient, and the rate and time-course of administration, will depend on the nature of the subject, the nature and severity of the condition, the administration method used, etc... Appropriate values can be selected by the trained medical practitioner. The compound may be administered alone or in combination with other treatments, either simultaneously or sequentially. It may be administered by any suitable route, including orally, intravenously, cutaneously, subcutaneously, parenterally, nasally, intramuscularly, intraperitoneally, etc... It may be administered directly to a suitable site or in a manner in which it targets a particular site, such as a certain type of cell - suitable targeting methods are already known.

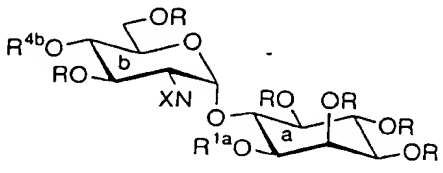
A diagnostic method according to the invention might

involve the use of one of the compounds (which of course includes antagonists), or of a specific binding partner for it, or of a species which competes with it in binding to another specific binding partner, to determine, either qualitatively or quantitatively, the existence of a particular medical condition or change in condition. Such a method may be carried out either *in vitro* or *in vivo*. One or more of the materials used in the method may be appropriately labelled.

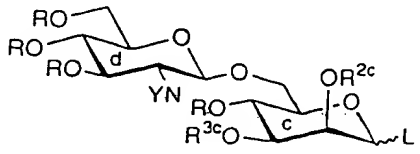
A seventh aspect of the present invention provides a method of preparation of a pharmaceutical composition, involving admixing one or more of the compounds with one or more pharmaceutically acceptable adjuvants, and/or with one or more other therapeutically active agents.

Synthesis of the Compounds

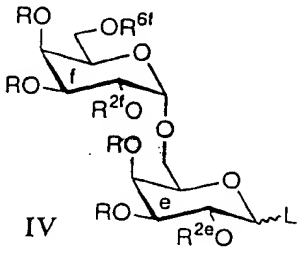
Further aspects of the present invention relate to the synthesis of compounds of formula I. The preferred strategy allows their preparation from four readily available monosaccharide units, via three intermediate disaccharide "building blocks". These disaccharide intermediates have the general formulae II, III and IV:



II



III



IV

in which R, X and Y have the same meanings as in formula I, and each L is a leaving group (or "activating group") which activates the anomeric position of the relevant saccharide unit in preparation for a glycosylation reaction with a glycosyl acceptor, or alternatively a leaving group precursor (ie, a group which can be converted into a suitable leaving group). Each L must be chosen to ensure the optimum balance between reactivity at the anomeric position and selectivity in the unit as a whole, depending on the reactions which the unit in question is to undergo.

The constituent saccharide units of compounds II-IV are again labelled a-f, to reflect their correspondence with the units in formula I.

In compound II, position 1 of unit a is ideally differentiated from the other positions of that unit by the choice of appropriate R groups. For instance, R^{1a} may be MntCO and the rest of the unit may be protected as a dicyclohexylidene acetal in which R^{2a} and R^{3a}, and separately R^{4a} and R^{5a}, together represent the bridging

group *O*-cyclohexylidene. X is preferably N_2. R^{4b} is conveniently H, or a removable precursor group such as TBDMS, in preparation for a subsequent glycosylation of II. R^{3b} and R^{6b} may be protecting groups such as Bn.

In compound III, L is preferably trichloroacetimidate ($C(NH)CCl_3$) or a leaving group precursor such as thiophenyl (SPh). SPh is a preferred leaving group precursor because of its stability and its versatility, being readily convertible into a number of suitable leaving groups. R^{2c} needs to be a permanent, non-participating group, preferably Bn. Suitable groups for R^{3c} and R^{4c} include Bn and TBDPS, preferably Bn for R^{4c} and TBDPS for R^{3c}. R^{3c} should preferably differ from R^{2c} and R^{4c}. In unit d, NY must be a participating group, preferably NPht, and suitable protecting groups R include an acetal bridging group such as benzylidene acetal for positions 4 and 6, and Bn for position 3.

In compound IV, L is preferably trichloroacetimidate or a leaving group precursor such as thiophenyl. The R groups at positions 2, 3 and 4 of both units and position 6 of unit f are suitable protecting groups such as Bn, Ac or (ideally for positions 3 and 4 in each unit) a bridging acetal such as *O*-isopropylidene. However R^{2e} and R^{2f} must be permanent non-participating protecting groups

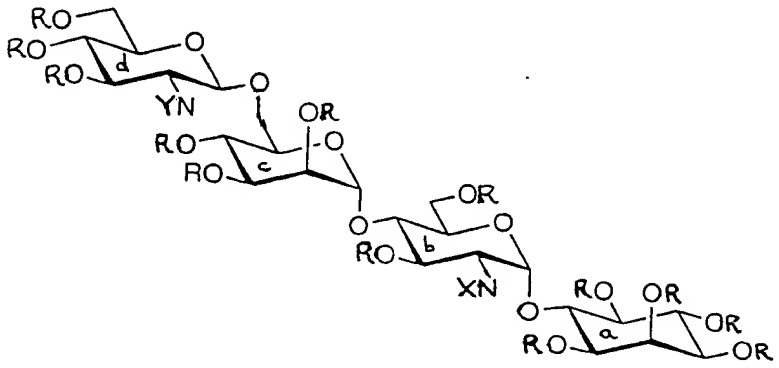
such as Bn, and R^{6f} must be a temporary protecting group chosen to permit orthogonal deprotection with respect to all permanent protecting groups in the final product I.

Accordingly, the eighth aspect of the present invention provides a method of synthesis of a compound of formula I, which involves the use, and preferably also the preparation, of at least two of the intermediate disaccharide compounds II, III and IV. This method conveniently involves condensing together the at least two disaccharides to form a tetrasaccharide intermediate compound. The hexasaccharide product is preferably synthesised by reacting the tetrasaccharide intermediate with a third disaccharide intermediate, preferably also selected from compounds II, III and IV. The method preferably involves reacting together at least compounds II and III, more preferably all three compounds II, III and IV.

The method optionally includes the removal, after formation of the hexasaccharide, of one or more protecting groups R, and/or their replacement with other groups such as phosphates, for instance to produce the compound 1. Conventional chemical techniques may be used to effect such substituent changes, the nature and sequence of the reaction steps used depending on the

nature of the R groups and on the groups with which they are to be replaced.

Preferably, compounds II and III are reacted together first, to form an intermediate tetrasaccharide of the general formula XI:



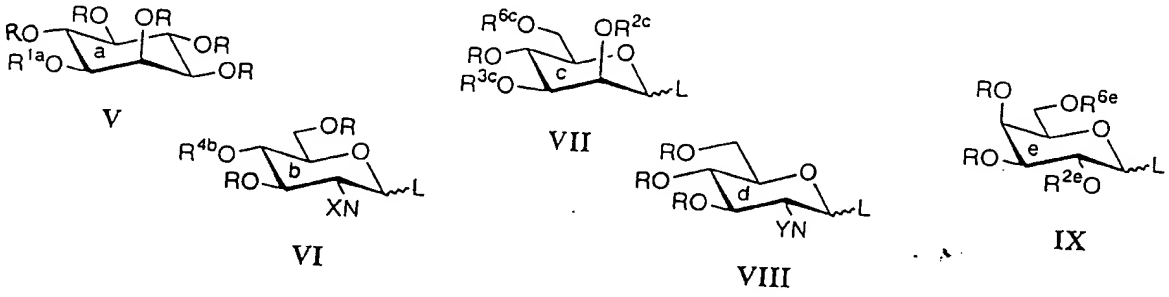
in which R, X and Y are as defined in connection with compounds II and III, and R^{3c} is preferably hydrogen.

Compound XI is then preferably glycosylated using compound IV as a glycosyl donor, to form compound I. This last step will involve the selective deprotection of compound XI at R^{3c} to convert it into a glycosyl acceptor.

A ninth aspect of the invention therefore provides a method of synthesis of a compound of formula I, which involves the use, preferably also the preparation, of a tetrasaccharide intermediate of the formula XI and preferably the reaction of that intermediate with a compound of formula IV.

Compounds II, III and IV are preferably prepared

from the monosaccharide "building blocks" represented by the general formulae V-IX:



in which R, X, Y and L have the same meanings as in formulae II-IV, the units again bearing letters corresponding to those which they will provide in compounds I-IV (although compound IX provides both units e and f in compound IV).

Compound II is preferably prepared by firstly preparing the *myo*-inositol building block V and then glycosylating using a D-glucosamine derivative such as VI as a glycosyl donor. In the *myo*-inositol building block, position 6 should be free for glycosylation (ie, R^{6a} should be hydrogen) and position 1 should ideally be differentiated, as explained in connection with compound II. Compound V may be prepared from *myo*-inositol using a regioselective acylation reaction via a boron-tin exchange reaction [25-30].

The glycosyl donor is preferably a 2-azido-2-deoxy-

D-glucopyranosyl, ie, compound VI with $X=N_2$. L is preferably a trichloroacetimidate leaving group, which may be precursed during the synthesis by for instance a thiophenyl group. Such a compound may be prepared, for instance, from a 2-amino-2-deoxy D-glucosamine hydrochloride, via a diazo transfer reaction from trifluoromethanesulphonyl azide [37].

R^{3b}, R^{4b} and R^{6b} in the glycosyl donor may be any suitable protecting groups, such as Bn for R^{3b} and R^{6b} and TBDMS (selectively removable) for R^{4b}. Generally speaking, R^{4b} should be different to R^{3b} and R^{6b}, and more preferably R^{3b} and R^{6b} are the same. Bridging acetals are not preferred as protecting groups since their subsequent reductive opening, during the glycosylation reaction, can lead to hydrolysis of acetal protecting groups present on the *myo*-inositol unit. Since in compound II, R^{4b} should ultimately be H, position 4b should be selectively deprotected following glycosylation of the *myo*-inositol block.

Compound III is preferably prepared by glycosylating the mannose derivative VII, with the glucosamine derivative VIII. In VII, L is ideally a leaving group precursor such as thiophenyl, which can be converted to a suitable leaving group following glycosylation with VIII.

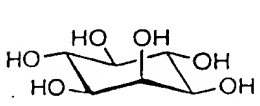
R^{6c} should ultimately be hydrogen, leaving that position free for glycosylation. Suitable groups for R^{2c}, R^{3c} and R^{4c} include Bn and TBDPS, preferably Bn for R^{2c} and R^{4c} and TBDPS for R^{3c}. R^{2c} needs to be permanent and non-participating, as in III. R^{3c} and R^{6c} are mutually orthogonal temporary protecting groups chosen to allow deprotection without affecting the remaining groups at positions 1 and 4.

In the glucosamine derivative VIII used as the glycosyl donor, positions 3, 4 and 6 must be protected, whilst L must be a suitable leaving group, fluoride being preferred. Suitable protecting groups include an acetal bridging group such as benzylidene acetal for positions 4 and 6, and Bn for position 3. NY must be a participating group such as NPht.

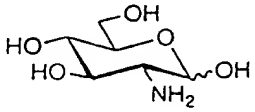
Compound IV is preferably prepared by reacting together a D-galactose-based glycosyl donor and acceptor, both corresponding to formula IX, both of which can be prepared from appropriate D-galactose derivatives such as β-D-galactopyranose pentaacetate. In compound IX, for the glycosyl donor, L is a suitable leaving group such as trichloroacetimidate and R^{2e}, R^{3e}, R^{4e} and R^{6e} represent suitable protecting groups such as Bn, Ac or (ideally for positions 3 and 4) a bridging acetal such as O-

isopropylidene. For the glycosyl acceptor, R^{6e} should be hydrogen ready for glycosylation, whilst positions 2, 3 and 4 must be suitably protected such as with Bn or (again conveniently for positions 3 and 4) a bridging acetal such as *O*-isopropylidene. L must be a leaving group precursor, preferably a thiophenyl group. One limitation on the substituents is that R^{2e} in both the glycosyl donor and acceptor must be a permanent non-participating group, Bn being preferred for both.

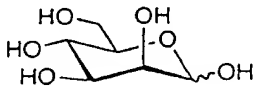
Thus, the methods of the invention can be seen more preferably to involve preparing the intermediate compounds II, III and IV starting from the four monosaccharide units *myo*-inositol, D-glucosamine, D-mannose and β-D-galactose, any of which may be in the form of a derivative such as a pentaacetate in which, for instance, one or more hydroxyl groups have been replaced by suitable protecting groups. The preferred four starting materials are:



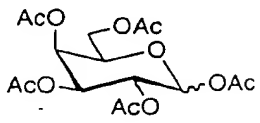
myo-inositol



D-glucosamine



D-mannose



β-D-galactopyranose pentaacetate

Accordingly, a tenth aspect of the invention

provides a method of synthesis of a compound of formula I, which involves the use of *myo*-inositol, D-glucosamine, D-mannose and β-D-galactose, and/or of suitable derivatives thereof, as the basic monosaccharide starting materials. β-D-galactopyranose pentaacetate is preferably used in place of β-D-galactose itself.

Clearly the protecting groups used during the synthesis must be carefully chosen so as to ensure availability only of the appropriate substituents at any given time. Suitable groups are referred to above in connection with the compounds II-IX.

The substituents referred to as preferred in compounds V-IX and/or in compounds II-IV are of course also preferred, in the corresponding positions, in the tetrasaccharide intermediate XI and in the final product I.

Many of the intermediate compounds formed during a synthesis according to the invention are believed to be novel compounds. These include compounds **9**, **10**, **11**, **12**, **13**, **18**, **19**, **24**, **25**, **26**, **27**, **28**, **29**, **30**, **31**, **32**, **35**, **36**, **37**, **38**, **39**, **40**, **41**, **42** and **43** referred to in the Example below. In particular, an eleventh aspect of the invention provides a compound of the general formula II,

or a salt or other derivative thereof, in which R^{4b} (which is preferably hydrogen, or a protecting group chosen to permit orthogonal deprotection with respect to the other protecting groups present) is different to R^{3b} and preferably also to R^{6b}, and more preferably R^{3b} and R^{6b} are the same as each other but different to R^{4b}.

Twelfth to eighteenth aspects of the invention provide, respectively, compounds of the general formulae III, IV, VI to IX and XI, as defined above, or in each case a salt or other derivative thereof.

A nineteenth aspect of the present invention provides a method of synthesis of a compound of formula II (as defined above), which involves firstly preparing a glycosyl donor, in the form of a 2-azido-2-deoxy-D-glucopyranosyl of formula VI (with $X=N_2$), from a 2-amino-2-deoxy D-glucosamine salt via a diazo transfer reaction from trifluoromethanesulphonyl azide (as shown in Figure 4), and then reacting that donor with a glycosyl acceptor in the form of a *myo*-inositol building block of formula V. The method preferably also involves preparing compound V. The nature of the R and L groups are preferably as described above in connection with the preparation of intermediate II. In particular, R^{4b} is preferably differentiated from the other R groups of the glycosyl

donor, so that in the product II position 4b is free for further glycosylation, for instance for use in the synthesis of the tetrasaccharide XI and/or the hexasaccharide I.

Finally, a twentieth aspect of the invention provides a method of synthesis of a tetrasaccharide of the general formula XI, as defined above, by reacting together a glycosyl acceptor of formula II, in which R^{4b} is hydrogen, and a glycosyl donor of formula III, in which L is a leaving group. The method preferably also involves preparing one or both of the compounds II and III; more preferably it involves preparing compound II in accordance with the nineteenth aspect of the invention.

Brief Description of the Drawings

Figure 1 shows the chemical formulae for (1) a preferred hexasaccharide according to the first aspect of the invention and (2) GPI anchors typically present in cell membranes;

Figure 2 shows a retrosynthetic analysis from which the methods of synthesis of the eighth to tenth aspects of the invention were derived; and

Figures 3-8 illustrate reaction schemes for a method of synthesis in accordance with the invention.

Example

There is now described an example synthesis, according to the present invention, of a compound of formula I.

The synthesis was devised using the retrosynthetic analysis depicted in Figure 2. It proceeded via three intermediate disaccharide compounds shown as II, III and IV, which themselves could be prepared (via monosaccharide units V-IX) from the four starting materials *myo*-inositol, D-glucosamine, D-mannose and β-D-galactopyranose pentaacetate.

Of note is the choice of protecting groups and leaving groups for the monosaccharide "building blocks" V-IX, to ensure the selective reaction of appropriate substituents during each stage of the synthesis and the desired stereochemistry at each glycosidic link formed.

Preparation of intermediate II

Figures 3-5 illustrate the preparation of disaccharide II from *myo*-inositol and D-glucosamine. A *myo*-inositol building block **6** was prepared following a previously reported procedure [25, 26] that is based on the well established regioselective enhancement of the nucleophilicity of hydroxyl groups as tributyl tin ethers

or dibutyl tin acetals [27], but overcoming the insolubility of *myo*-inositol in most organic solvents by using a boron-tin exchange reaction [28-30] (see also [24] for background on the preparation of *myo*-inositol derivatives).

Thus, *myo*-inositol was converted into the hexane soluble hexa-*O*-diethylboryl derivative **3** (100% yield), which was reacted *in situ* with dibutyl tin *bis*-acetylacetonate and then with L-menthyl chloroformate to give a diastereomeric mixture of regioselectively monosubstituted derivatives **4** and **5**, from which the desired diastereoisomer **4** could be separated. **4** was then transformed into the building block **6**, leaving position 6 free for glycosylation and position 1 differentiated, after protection as a dicyclohexylidene acetal.

Cyclohexylidene acetals of *myo*-inositol have been frequently used as intermediates in the preparation of glycosyl *myo*-inositols [31, 32]. Compound **6** was most conveniently prepared using 1-ethoxycyclohexene for the acetalation reaction, in cyclohexanone under conditions of thermodynamic control.

The 1,2-*cis* glycosylation of **6** was conveniently carried out using a 2-azido-2-deoxy-D-glucopyranosyl

trichloroacetimidate as the glycosyl donor. 2-azido-2-deoxy-glycosyl donors are currently employed in oligosaccharide syntheses but most of the methods used for the preparation of the 2-azido-2-deoxy building blocks involve low diastereoselectivity and a large number of steps [33-36]. In [37] there is however reported a "one-pot" synthesis of peracetylated 2-azido-2-deoxy sugars from commercially available 2-amino-2-deoxy sugar hydrochlorides through a diazo transfer reaction from trifluoromethanesulphonyl azide, and this method can be used to prepare the glycosyl donors **14** and **16** as shown in Figure 4.

D-glucosamine hydrochloride was thus converted [37] into the tetra-*O*-acetylated 2-azido-2-deoxy derivative **7**, which in turn was converted into the thioglycoside **8** [38]. Using well established chemical techniques [18, 23, 39-43], **8** was transformed into the trichloroacetimidates **14** and **16**, via the intermediates **9**, **10**, **11**, **12** and **13**, and **9**, **10** and **15**, respectively (see "Materials and Methods").

Glycosylation of the *myo*-inositol building block **6** with glycosyl donor **16** in the presence of trimethylsilyl triflate in diethyl ether [23] afforded **17** as a 10:1 α/β

mixture in 95% yield (Figure 5). The subsequent reductive opening of the benzylidene acetal [41] in this mixture, however, resulted in partial hydrolysis of the cyclohexylidene acetals; the donor **14** was therefore preferred for the glycosylation to prepare intermediate compound II.

Thus, **14** was condensed with **6** under the conditions mentioned above, as shown in Figure 5, to give **18** (corresponding to intermediate II) as a 9:1 α/β mixture in 73% yield. Treatment of **18** with tetrabutyl ammonium fluoride [44] afforded the product **19** (with position 4 of the glucosamine unit deprotected) in 83% yield.

Preparation of intermediate III

Referring now to Figure 6, compound III was prepared from the readily available mannose derivative, 1,6-anhydro-β-D-mannopyranose (**20**), via the protected mannose unit **28** which was then glycosylated with the glucosamine fluoride derivative **29**. Conversion of **20** to **28** was carried out according to the method described in [36].

Glycosylation of **28** was conveniently performed according to the methodology reported in [47], which gave with excellent yield and selectivity the disaccharide **30**.

This was then converted [18, 19, 23] into the trichloroacetimidate **32** (ie, the intermediate III) via compound **31** (see "Materials and Methods").

Preparation of intermediate IV

Figure 7 illustrates the preparation of IV from the galactose derivative β-D-galactopyranose pentaacetate (**33**). This was converted [21, 38, 45] to the glycosyl acceptor **34**, which was also further converted, via **35** and **36** (see "Materials and Methods"), into the glycosyl donor **37**.

The glycosylation reaction of **34** and **37** afforded the disaccharide **38** as a 6:1 α/β mixture in 86% yield. This was further transformed [18, 19, 23] into the trichloroacetimidate **40** via **39** (see "Materials and Methods"). **40** corresponds to intermediate IV.

Combination of II, III and IV

Figure 8 shows the preparation of the hexasaccharide product **43** corresponding to compound I. Firstly disaccharides **19** (intermediate II) and **32** (intermediate III) were condensed together to give the tetrasaccharide **41**, with excellent stereoselectivity and an 81% yield. A

carefully controlled desilylation of **41** led with a good yield to the glycosyl acceptor **42** (corresponding to XI), which carries a hydroxyl group at position 3 of the D-mannose unit.

42 was then glycosylated with the trichloroacetimidate **40** (intermediate IV) to give the hexasaccharide **43** as a 6.5:1 α/β mixture in 83% yield.

Deprotection of 43

To reach the compound **1** from **43**, conventional methods may be used to remove each of the protecting groups. As an example, firstly R^{1a} might be removed using an excess of LiOH in THF/MrOH at room temperature. This would simultaneously remove the acetate group R^{6f}, and also cause partial opening of the phthalimido group in unit d. The phthalimido group could be cyclised again by treatment with Et_3N/Ac_2O, which would lead to acetylation of both R^{1a} and R^{6f}. The phthalimido group could then be removed, for instance using a large excess of ethylenediamine in *n*-butanol at 90°C, with subsequent acetylation of the resulting amine under the usual conditions. *O*-deacetylation would then give a diol (ie, R^{1a} and R^{6f} being H) which could be subjected to

phosphorylation using the phosphoramidite procedure. Finally, treatment with hydrogen in the presence of 10% Pd/C would yield the final deprotected product 1.

5

Materials and methods.- TLC was performed on precoated plates (Merck aluminium sheets silica 60 F_{254}, Art. no. 5554); detection was effected by observation under UV light (254 nm), then visualised using sulfuric acid or phosphomolybdic acid in EtOH followed by heating. Column chromatography was conducted with Silica Gel 60 (0.023-0.040 mm, E. Merck) using de flash procedure. Melting points were determined usin a Reicher Jung Thermovar apparatus and were uncorrected. Specific rotations were measured on a Perkin Elmer model 241 polarimeter. NMR spectra were recorded on Varian Gemini-200, XL-300 or Unity 500 spectrometer. Chemical shifts are expressed in ppm and refered to the residual signal of the solvent used. Microanalysis was carried out by the Analysis Department of the Instituto de Quícica Orgánica General (CSIC).

2,3:4,5-di-*O*-cyclohexyliden-1-*O*-(-)-menthoxycarbonyl-1D-*myo*-inositol (6). To a solution of 100 mg (0.276 mmol) of 1-*O*-(-) menthoxycarbonyl-*myo*-inositol[26] (4) and 5.7 mg (0.03 mmol) of dried *p*-TsOH in 2 mL of cyclohexanone at room temperature was added 350 mL (2.76 mmol) of 1-ethoxycyclohexene. The reaction mixture was stirred for 3 h 30 min, quenched with Et_3N and evaporated. Silica-gel column chromatography (hexane-EtOAc, 5:1) afforded 73 mg (50%) of 6. TLC: R_f (hexane-EtOAc, 4:1) = 0.26. Mp: 83-85 °C. $[\alpha]_D$ - 50.4° (*c* 1.0, $CHCl_3$). ^1H RMN ($CDCl_3$, 200 MHz) δ: 0.76 (d, 3H, CH_3 Ment), 0.88 (d, 3H, CH_3 Ment), 0.92 (d, 3H, CH_3 Ment), 1.00-1.13 (m, 1H, Ment), 1.37-1.76 (m, 22H, 16H ciclohex, 6H Ment), 1.92-2.00 (m, 1H, Ment), 2.07-2.11 (m, 1H, Ment), 2.70 (d, 1H, $J_{OH,6}$= 3.5 Hz, 1H, OH), 3.44 (dd, $J_{5,4}$= 10.5 Hz, $J_{5,6}$= 9.0 Hz, 1H, H-5), 3.85 (dd, $J_{4,5}$= 10.5 Hz, $J_{4,3}$= 7.9 Hz, 1H, H-4), 4.10-4.14 (m, 1H, H-6), 4.33 (dd, $J_{3,2}$= 6.2 Hz, $J_{3,4}$= 7.9 Hz, 1H, H-3), 4.54 (dt, 1H, Ment), 4.60 (dd, $J_{2,1}$= 4.5 Hz, $J_{2,3}$= 6,1 Hz, 1H, H-2), 4.79 (t, $J_{1,2}$= $J_{1,6}$= 4.6 Hz, 1H, H-1). ^{13}C RMN ($CDCl_3$, 50 MHz) δ: 16.6, 21.2, 22.4 , 23.7, 24.0, 24.1, 24.3 , 25.4, 25.5, 26.5, 31.9, 32.1, 34.5, 35.0, 36.9, 37.0, 37.2, 41.1, 47.4, 72.5, 73.7, 76.6, 78.3 , 79.1, 79.6, 111.6, 113.3, 154.3.

Phenyl 3,4,6 - tri - *O* - acetyl - 2 - azido - 2 - deoxy - 1 - thio - D - glucopyranoside (8). To a solution of 2.10 g (5.63 mmol) of 1,3,4,6-tetra-*O*-acetyl-2-azido-2-deoxy-D-glucopyranose in 45 mL of CH_2Cl_2 at room temperature was added 1.15 mL (11.25 mmol) of thiophenol and 3.12 mL (25.31 mmol) of boron trifluoride diethyl etherate. The reaction mixture was stirred for 8 days, diluted with CH_2Cl_2, washed with NaCl an dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **8** in 66% yield and 25% of recovered starting material. TLC: R_f (hexane-EtOAc, 3:1) = 0.27. ^1H NMR for 8α, taken from the spectra of the mixture of α and β, (200 MHz, $CDCl_3$) δ: 1.96 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 3.96 (dd, $J_{6a,6b}$ = 12.4 Hz, $J_{6a,5}$ = 2.2 Hz, 1H, H-6a), 4.02 (dd, $J_{2,3}$ = 10.6 Hz, $J_{2,1}$ = 5.7 Hz, 1H, H-2), 4.23 (dd, $J_{6b,6a}$ = 12.4 Hz, $J_{6b,5}$ = 5.1 Hz, 1H, H-6b), 4.53 (ddd, $J_{5,4}$ = 10.2 Hz, $J_{5,6b}$ = 5.1 Hz, $J_{5,6a}$ = 2.2 Hz, 1H, H-5), 4.96 (t, $J_{4,3}$ = $J_{4,5}$ = 10.1 Hz, 1H, H-4), 5.27 (dd, $J_{3,2}$ = 10.4 Hz, $J_{3,4}$ = 9.8 Hz, 1H, H-

3), 5.58 (d, $J_{1,2}$ = 5.7 Hz, 1H, H-1), 7.20-7.45 (m, 5H, ArH). ^{1}H NMR for 8β, taken from the spectra of the mixture of α and β. (200 MHz, $CDCl_3$) δ: 1.94 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 3.34 (t, $J_{2,3} = J_{2,1}$ = 10.1 Hz, 1H, H-2), 3.63 (ddd, $J_{5,4}$ = 9.8 Hz, $J_{5,6b}$ = 4.9 Hz, $J_{5,6a}$ = 2.6 Hz, 1H, H-5), 3.92-4.21 (m, 2H, H-6a, H-6b), 4.42 (d, $J_{1,2}$ = 10.1 Hz, 1H, H-1), 4.86 (t, $J_{4,3} = J_{4,5}$ = 9.7 Hz, 1H, H-4), 5.01 (t, $J_{3,2} = J_{3,4}$ = 9.7 Hz, 1H, H-3), 7.20-7.45 (m, 5H, ArH).

Phenyl 2 - azido - 4,6 - *O* - benzylidene - 2 - deoxy - 1 - thio - D - glucopyranoside (9). To a solution of 3.00 g (7.09 mmol) of 8 in 110 mL of MeOH at room temperature was added 5 mL of sodium methoxide in MeOH (0.3M). After 20 min. the solution was neutralized with Amberlite IR-120, filtrated and evaporated. The mixture of phenyl 2-azido-2-deoxy-1-thio-D-glucopyranosides obtained was dissolved, without any purification, in 30 mL of CH_3CN. 5.32 mL (35.45 mmol) of benzaldehyde dimethyl acetal and 67.4 mg (0.35 mmol) of p-toluensulfonic acid were added and the reaction mixture was stirred for 2 h, quenched with Et_3N and evaporated. Silica-gel column chromatography (hexane-EtOAc, 6:1) afforded 9α and 9β, in a ratio of 70:30 and overall yield of 97%. Data for 9α. TLC: R_f(hexane-EtOAc, 3:1) = 0.34. Mp: 127-128°C. $[\alpha]_D$ + 226.881° (*c* 1.09, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.90 (d, $J_{OH,3}$ = 2.0 Hz, 1H, OH), 3.58 (t, $J_{4,3} = J_{4,5}$ = 9.3 Hz, 1H, H-4), 3.76 (t, $J_{6a,5} = J_{6a,6b}$ = 10.2 Hz, 1H, H-6a), 3.92 (dd, $J_{2,3}$ = 9.8 Hz, $J_{2,1}$ = 5.4 Hz, 1H, H-2), 4.07 (dt, $J_{3,4} = J_{3,2}$ = 9.6 Hz, $J_{3,OH}$ = 2.0 Hz, 1H, H-3), 4.24 (dd, $J_{6b,6a}$ = 10.2 Hz, $J_{6b,5}$ = 4.9 Hz, 1H, H-6b), 4.41 (dt, $J_{5,4} = J_{5,6a}$ = 10.2 Hz, $J_{5,6b}$ = 4.9 Hz, 1H, H-5), 5.57 (s, 1H, H-7), 5.58 (d, $J_{1,2}$ = 5.4 Hz, 1H, H-1), 7.30-7.56 (m, 10H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 63.46, 63.91, 68.51, 70.72, 81.68, 87.81, 102.18, 126.19, 126.29, 128.01, 128.40, 129.18, 129.42, 132.47, 133.05, 136.80. Anal. Calcd. for $C_{19}H_{19}N_3O_4S$: C, 59.21; H, 4.97; N, 10.90; S, 8.32. Found: C, 59.13; H, 5.08; N, 10.71; S, 8.13. Data for 9β. TLC: R_f(hexane-EtOAc, 3:1) = 0.36. Mp: 152-154°C. $[\alpha]_D$ - 65.816° (*c* 0.96, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.88 (d, $J_{OH,3}$ = 2.1 Hz, 1H, OH), 3.35 (dd, $J_{2,1}$ = 10.2, $J_{2,3}$ = 9.0 Hz, 1H, H-2), 3.41-3.52 (m, 2H, H-4, H-5), 3.73 (dt, $J_{3,2} = J_{3,4}$ = 8.9 Hz, $J_{3,OH}$ = 2.1 Hz, 1H, H-3), 3.77 (t, $J_{6a,6b} = J_{6a,5}$ = 10.2 Hz, 1H, H-6a), 4.38 (dd, $J_{6b,6a}$ = 10.2 Hz, $J_{6b,5}$ = 4.4 Hz, 1H, H-6b), 4.52 (d, $J_{1,2}$ = 10.2 Hz, 1H, H-1), 5.53 (s, 1H, H-7), 7.35-7.61 (m, 10H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 65.20, 68.41, 70.27, 74.11, 80.22, 86.83, 101.94, 126.24, 128.38, 128.67, 129.12, 129.41, 130.88, 133.67, 136.74. Anal. Calcd. for $C_{19}H_{19}N_3O_4S$: C, 59.21; H, 4.97; N, 10.90; S, 8.32. Found: C, 59.09; H, 4.65; N, 10.81.

Phenyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-D-glucopyranoside (10). To a solution of 546 mg (1.42 mmol) of 9β in 9 mL of DMF at room temperature was added 43 mg (1.70 mmol) of sodium hydride and then 0.21 mL (2.84 mmol) of benzyl bromide. The reaction mixture was stirred for 40 min., quenched

with a saturated solution of $NaHCO_3$ and dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc) afforded **10β** in 98% yield. **10α** was synthesized using **9α** as starting material with a yield of 95%. Data for **10β**. TLC: R_f (hexane-EtOAc, 3:1) = 0.58. Mp: 106-108°C. $[\alpha]_D$ - 120.950° (*c* 0.93, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 3.38 (dd, $J_{2,1}$ = 10.2, $J_{2,3}$ = 9.1 Hz, 1H, H-2), 3.45 (m, 1H, H-5), 3.60-3.69 (m, 2H, H-3, H-4), 3.81 (t, $J_{6a,6b} = J_{6a,5}$ = 10.2 Hz, 1H, H-6a), 4.41 (dd, $J_{6b,6a}$ = 10.2 Hz, $J_{6b,5}$ = 4.9 Hz, 1H, H-6b), 4.51 (d, $J_{1,2}$ = 10.2 Hz, 1H, H-1), 4.87 (dd, 2H, CH_2Ph), 5.59 (s, 1H, H-7), 7.31-7.61 (m, 15H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 64.75, 68.50, 70.50, 75.19, 80.97, 81.31, 86.67, 101.29, 125.97, 128.00, 128.30, 128.42, 128.72, 129.11, 133.92, 137.09, 137.58. Anal. Calcd. for $C_{26}H_{25}N_3O_4S$: C, 65.67; H, 5.30; N, 8.84; S, 6.74. Found: C, 65.91 H, 5.21; N, 8.52; S, 6.58. Data for **10**. TLC: R_f (hexane-EtOAc, 3:1) = 0.54. Mp: 145-147°C. $[\alpha]_D$ + 125.552° (*c* 0.74, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 3.73-3.83 (m, 1H, H-4), 3.78 (t, $J_{6a,6b} = J_{6a,5}$ = 10.3 Hz, 1H, H-6a), 3.92-4.04 (m, 2H, H-2, H-3), 4.24 (dd, $J_{6b,6a}$ = 10.3 Hz, $J_{6b,5}$ = 5.0 Hz, 1H, H-6b), 4.44 (dt, $J_{5,4} = J_{5,6a}$ = 10.3 Hz, $J_{5,6b}$ = 5.0 Hz, 1H, H-5), 4.92 (dd, 2H, CH_2Ph), 5.58 (m, 1H, H-1), 5.62 (s, 1H, H-7), 7.30-7.53 (m, 15H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 63.61, 63.84, 68.60, 75.18, 77.82, 82.74, 87.90, 101.51, 126.01, 127.95, 128.23, 128.30, 128.42, 129.09, 129.17, 132.47, 133.01, 137.12, 137.67. Anal. Calcd. for $C_{26}H_{25}N_3O_4S$: C, 65.67; H, 5.30; N, 8.84; S, 6.74. Found: C, 65.50; H, 5.12; N, 8.68; S, 6.42.

Phenyl 2 - azido - 3, 6 - di - *O* - benzyl - 2 - deoxy - 1 - thio - D - glucopyranoside (11). A solution of 447 mg (0.94 mmol) of **10β** in 9.4 mL of THF containing 3Å molecular sieves was stirred for 30 min. at room temperature; after this, 1.201 g (18.16 mmol) of sodium cyanoborohydride was added. A saturated solution of hydrogen chloride in diethyl ether was then added dropwise until the evolution of gas had ceased (pH < 7) and a TLC analysis showed conversion of all the starting material. The mixture was neutralized with a saturated solution of $NaHCO_3$ in water, diluted with CH_2Cl_2, filtrated through celite, washed with water and dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **11β** in 96% yield. **11α** was synthesized using **10α** as starting material with a yield of 87%. Data for **11β**. TLC: R_f (hexane-EtOAc, 3:1) = 0.28. $[\alpha]_D$ - 64.151° (*c* 1.10, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 2.70 (d, $J_{OH,4}$ = 2.4 Hz, 1H, OH), 3.27-3.41 (m (ABX), 2H, H-2, H-3), 3.47 (m, 1H, H-5), 3.65 (dt, $J_{4,3} = J_{4,5}$ = 8.5 Hz, $J_{4,OH}$ = 2.4 Hz, 1H, H-4), 3.75 (dd, $J_{6a,6b}$ = 10.4 Hz, $J_{6a,5}$ = 4.3 Hz, 1H, H-6a), 3.81 (dd, $J_{6b,6a}$ = 10.4 Hz, $J_{6b,5}$ = 4.9 Hz, 1H, H-6b), 4.45 (m (ABX), $J_{1,2}$ = 9.9 Hz, 1H, H-1), 4.59 (dd, 2H, CH_2Ph), 4.87 (dd, 2H, CH_2Ph), 7.28-7.61 (m, 15H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 64.55, 70.27, 71.88, 73.72, 75.42, 78.05, 84.60, 86.23, 127.66, 127.82, 128.08, 128.17, 128.33, 128.45, 128.59, 128.96, 131.29, 133.48, 137.71, 137.86. Anal. Calcd. for $C_{26}H_{27}N_3O_4S$: C, 65.39; H, 5.70; N, 8.80; S, 6.71. Found: C, 65.61; H,

5.35; N, 8.58; S, 6.35. Data for **11α**. TLC: R_f (hexane-EtOAc, 3:1) = 0.31. $[\alpha]_D$ + 124.866° (*c* 1.34, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 2.51 (d, $J_{OH,4}$ = 2.7 Hz, 1H, OH), 3.62-3.75 (m, 3H, H-3, H-6a, H-6b), 3.77 (dt, $J_{4,3} = J_{4,5}$ = 8.0 Hz, $J_{4,OH}$ = 2.7 Hz, 1H, H-4), 3.92 (dd, $J_{2,3}$ = 10.0 Hz, $J_{2,1}$ = 5.4 Hz, 1H, H-2), 4.35 (m, 1H, H-5), 4.56 (dd, 2H, CH_2Ph), 4.91 (dd, 2H, CH_2Ph), 5.58 (d, $J_{2,1}$ = 5.4 Hz, 1H, H-1), 7.25-7.54 (m, 15H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 63.59, 69.72, 71.05, 72.36, 73.63, 75.39, 81.32, 87.28, 127.68, 127.80, 128.11, 128.17, 128.43, 128.65, 129.05, 132.16, 133.43, 137.71, 137.95. Anal. Calcd. for $C_{26}H_{27}N_3O_4S$: C, 65.39; H, 5.70; N, 8.80; S, 6.71. Found: C, 65.74; H, 6.05; N, 8.81; S, 6.60.

Phenyl 2-azido-3,6-di-*O*-benzyl-4-*O*-(tert-butyldimethylsilyl)-2-deoxy-1-thio-D-glucopyranoside (12). A solution of 345 mg (0.72 mmol) of **11β** and 287 μL (2.17 mmol) of collidine in 1 mL of CH_2Cl_2 was cooled at 0°C. 249 μL (1.08 mmol) of *tert*-butyldimethylsilyltriflate were added dropwise during 2 h. The mixture was stirred 10 min and quenched with water/ice, diluted and extracted with CH_2Cl_2, washed with brine and dried over Na_2SO_4. Silica-gel column chromatography afforded **12β** in 95% yield. **12α** was synthesized using **11α** as starting material with a yield of 98%. Data for **12β**. TLC: R_f (hexane-EtOAc, 5:1) = 0.69. $[\alpha]_D$ - 0.231° (*c* 0.65, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 0.01 (s, 3H, CH_3), 0.03 (s, 3H, CH_3), 0.88 (s, 9H, ^{t}Bu), 3.24-3.40 (m (ABX), 2H, H-2, H-3), 3.45 (m, 1H, H-5), 3.57-3.68 (m, 1H, H-4), 3.64 (dd, $J_{6a,6b}$ = 10.7 Hz, $J_{6a,5}$ = 5.4 Hz, 1H, H-6a), 3.78 (dd, $J_{6b,6a}$ = 10.7 Hz, $J_{6b,5}$ = 2.1 Hz, 1H, H-6b), 4.50 (m (ABX), $J_{1,2}$ = 9.7 Hz, 1H, H-1), 4.59 (dd, 2H, CH_2Ph), 4.84 (dd, 2H, CH_2Ph), 7.20-7.66 (m, 15H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: -4.74, -3.78, 17.98, 25.91, 65.74, 69.12, 70.55, 73.37, 75.57, 80.70, 85.48, 86.49, 127.51, 127.59, 128.11, 128.33, 128.97, 131.71, 133.71, 137.98, 138.37. Anal. Calcd. for $C_{32}H_{41}N_3O_4SSi$: C, 64.94; H, 6.98; N, 7.10; S, 5.42. Found: C, 65.45; H, 7.00; N, 6.96; S, 5.32. Data for **12α**. TLC: R_f (hexane-EtOAc, 5:1) = 0.62. $[\alpha]_D$ + 160.004° (*c* 1.38, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 0.02 (s, 3H, CH_3), 0.05 (s, 3H, CH_3), 0.90 (s, 9H, ^{t}Bu), 3.58 (dd, $J_{3,2}$ = 10.1Hz, $J_{3,4}$ = 8.4 Hz, 1H, H-3), 3.71 (bd, *J* = 3.8 Hz, 2H, H-6a, H-6b), 3.74 (Ψt, $J_{4,3}$ = 8.4 Hz, $J_{4,5}$ = 9.4 Hz, 1H, H-4), 3.95 (dd, $J_{2,3} \cong$ 10.1 Hz, $J_{2,1}$ = 5.4 Hz, 1H, H-2), 4.37 (dt, $J_{5,4}$ = 9.4 Hz, $J_{5,6a} = J_{5,6b}$ = 3.8 Hz, 1H, H-5), 4.55 (dd, 2H, CH_2Ph), 4.87 (dd, 2H, CH_2Ph), 5.63 (d, $J_{1,2}$ = 5.4 Hz, 1H, H-1), 7.21-7.61 (m, 15H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: -4.75, -3.71, 18.03, 25.94, 64.78, 68.91, 71.29, 73.13, 73.17, 75.20, 81.84, 87.41, 127.30, 127.47, 127.70, 128.27, 129.01, 132.44, 133.62, 138.06, 138.15. Anal. Calcd. for $C_{32}H_{41}N_3O_4SSi$: C, 64.94; H, 6.98; N, 7.10; S, 5.42. Found: C, 65.26; H, 6.77; N, 7.20; S, 5.50.

2-azido-3,6-di-*O*-benzyl-4-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-glucopyranose (13). A solution of 331 mg (0.56 mmol) of **12β** in 12 mL of acetone was cooled to -15°C in darkness. Then 129 mg (0.73 mmol) of *N*-bromosuccinimide

were added. After 45 min. the reaction mixture was quenched with a saturated solution of $NaHCO_3$ in water, diluted and extracted with EtOAc, washed with brine and dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 7:1) afforded **13**, as a mixture of α and β (11:1) isomers, in quantitative yield. The same procedure was used for **12α**. TLC: R_f(hexane-EtOAc, 6:1) = 0.15. M.p.: 76-78°C. ^{1}H NMR for **13α** (200 MHz, $CDCl_3$) δ: -0.04 (s, 3H, CH_3), -0.03 (s, 3H, CH_3), 0.84 (s, 9H, ^{t}Bu), 3.35 (dd, $J_{2,3}$ = 10.1 Hz, $J_{2,1}$ = 3.5 Hz, 1H, H-2), 3.49 (dd, $J_{6a,6b}$ = 10.1 Hz, $J_{6a,5}$ = 6.9 Hz, 1H, H-6a), 3.54 (dd, $J_{4,3}$ = 8.5 Hz, $J_{4,5}$ = 9.7 Hz, 1H, H-4), 3.69 (dd, $J_{6b,6a}$ = 10.1 Hz, $J_{6b,5}$ = 2.1 Hz, 1H, H-6b), 3.81 (dd, $J_{3,2}$ = 10.1 Hz, $J_{3,4}$ = 8.5 Hz, 1H, H-3), 4.04-4.14 (m, 1H, H-5), 4.59 (dd, 2H, CH_2Ph), 4.84 (dd, 2H, CH_2Ph), 5.37 (bd, J = 3.2 Hz, 1H, H-1), 7.28-7.41 (m, 10H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: -4.81, -4.74, -3.75, 17.93, 25.85, 64.45, 67.78, 69.25, 71.16, 71.65, 71.83, 73.34, 73.47, 74.99, 76.07, 77.18, 80.11, 83.10, 92.05, 96.30, 127.38, 127.44, 127.66, 127.77, 127.91, 128.22, 128.42, 137.71, 138.15. Anal. Calcd. for $C_{26}H_{37}N_3O_5Si$: C, 62.50; H, 7.46; N, 8.41. Found: C, 62.80; H, 7.08; N, 8.15.

2-azido-3,6-di-*O*-benzyl-4-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-glucopyranosyl trichloracetimidate (14). To a solution of 241 mg (0.48 mmol) of **13** in 2.5 mL of CH_2Cl_2 at room temperature, were added 484 μL (4.83 mmol) of trichloracetonitrile and 67 mg (0.48 mmol) of activated potasium carbonate. After 1 h 45 min. the reaction mixture was diluted with CH_2Cl_2, filtrated through celite and evaporated. Silica-gel column chromatography (hexane-EtOAc, 10:1) afforded **14α** and **14β**, in a ratio of 3:7 and overall yield of 91%. Data for **14β**. TLC: R_f(hexane-EtOAc, 6:1) = 0.43. $[\alpha]_D$+28.528° (*c* 2.10, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.07 (s, 3H, CH_3), 0.09 (s, 3H, CH_3), 0.87 (s, 9H, ^{t}Bu), 3.35 (dd, J = 9.6 Hz, J = 8.4 Hz, 1H, H-4), 3.54-3.83 (m, 4H, H-3, H-5, H-6a, H-6b), 3.69 (dd, $J_{2,3}$ = 10.6 Hz, $J_{2,1}$ = 8.3 Hz, 1H, H-2), 4.59 (dd, 2H, CH_2Ph), 4.86 (dd, 2H, CH_2Ph), 5.71 (d, $J_{1,2}$ = 8.3 Hz, 1H, H-1), 7.28-7.40 (m, 10H, ArH), 8.80 (s, 1H, NH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: -4.82, -3.83, 18.00, 25.92, 66.13, 68.27, 70.28, 73.23, 75.07, 77.64, 83.42, 96.95, 127.36, 127.47, 127.54, 128.30, 138.15, 138.34, 161.01. Data for **14α**. TLC: R_f(hexane-EtOAc, 6:1) = 0.38. $[\alpha]_D$+94.704° (*c* 1.38, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.06 (s, 3H, CH_3), 0.08 (s, 3H, CH_3), 0.90 (s, 9H, ^{t}Bu), 3.65-3.95 (m, 6H, H-2, H-3, H-4, H-5, H-6a, H-6b), 4.57 (dd, 2H, CH_2Ph), 4.89 (dd, 2H, CH_2Ph), 6.50 (d, $J_{1,2}$ = 3.4 Hz, 1H, H-1), 7.32-7.41 (m, 10H, ArH), 8.75 (s, 1H, NH). ^{13}C NMR (50 MHz, $CDCl_3$) δ:-4.83, -3.76, 18.00, 25.94, 63.68, 68.24, 70.48, 73.26, 74.90, 75.07, 80.38, 94.98, 127.34, 127.48, 128.22, 128.26, 137.90, 138.12, 160.81. Anal. Calcd. for $C_{28}H_{37}Cl_3N_4O_5Si$: C, 52.22; H, 5.79; N, 8.70. Found: C, 52.51; H, 5.45; N, 8.48.

2-azido-3-*O*-bencyl-4,6-*O*-bencylidene-2-deoxy-D-glucopyranose (15). To a solution of 80 mg (0.168 mmol) of **10α** in 1.7 mL of aceton was cooled at

-15 °C in darkness. Then 51.5 mg (0.289 mmol) of NBS were added. After 1 h 15 min the reaction mixture was quenched with a saturated solution of $NaHCO_3$ in water, diluted and extracted with EtOAc, washed with brine and dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 2:1), afforded 62 mg (96%) as a mixture of α/β (1:1) isomers. TLC: R_f(hexane-EtOAc, 2:1) = 0.41; M.p.: 115-117 °C. ^{1}H RMN ($CDCl_3$, 200 MHz) δ: 3.08 (d ancho, $J_{OH,1}$= 3.0 Hz, 1H, OH), 3.31 (dd, $J_{2,1}$= 7.7 Hz, $J_{2,3}$= 8.8 Hz, 1H, H-2β), 3.30-3.37 (m, 1H, H-5β), 3.39 (dd, $J_{2,1}$= 3.7 Hz, $J_{2,3}$= 10.0 Hz, 1H, H-2α), 3.51 (t, $J_{4,3}$= $J_{4,5}$= 9.2 Hz, 1H, H-4β), 3.60-3.73 (m, 4H, H-3β, H-6β, 2Hα), 3.98-4.07 (m, 2H, Hα), 4.20 (dd, $J_{6,5}$= 4.9 Hz, $J_{6,6'}$= 10.3 Hz, 1H, H-6), 4.24 (dd, $J_{6,5}$= 5.0 Hz, $J_{6,6'}$= 10.5 Hz, 1H, H-6), 4.50 (bdd, $J_{1,OH}$= 3.1 Hz, $J_{1,2}$= 7.8 Hz, 1H, H-1b), 4.78 (dd, 2H, $CH_2Ph\beta$), 4.80 (dd, 2H, $CH_2Ph\alpha$), 5.16 (bt, $J_{1,2}$= $J_{1,OH}$= 3.1 Hz, 1H, H-1α), 5.49 (s, 1H, H-7β), 5.51 (s, 1H, H-7α), 7.16-7.44 (m, 10H, ArH). ^{13}C RMN ($CDCl_3$, 50 MHz) δ: 62.7, 63.5, 66.3, 67.2, 68.4, 68.9, 74.9, 75.1, 76.2, 79.0, 81.4, 82.7, 92.7 (C-1α), 96.4 (C-1β), 101.3 (C-7), 101.4 (C-7), 125.9, 126.0, 127.9, 128.2, 128.3, 128.4, 129.1, 137.0, 137.1, 137.7.

2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-D-glucopyranosyl trichloracetimidate (16). To a solution of 177 mg (0.46 mmol) of **15** in 2.5 mL of CH_2Cl_2 at room temperature, were added 463 μL (4.62 mmol) of trichloracetonitrile and 64 mg (0.46 mmol) of activated potasium carbonate. After 1 h 30 min. the reaction mixture was diluted with CH_2Cl_2, filtrated through celite and evaporated. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **15**α and **15**β, in a ratio of 1:10 and overall yield of 92%. Data for **16**β. TLC: R_f(hexane-EtOAc, 4:1) = 0.45. $[\alpha]_D$ -59.902° (*c* 0.99, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.56-3.89 (m, 5H, H-2, H-3, H-4, H-5, H-6'), 4.41 (dd, $J_{6,5}$= 4.8 Hz, $J_{6,6'}$= 10.5 Hz, 1H, H-6), 4.90 (dd, 2H, CH_2Ph), 5.60 (s, 1H, H-7), 5.70-5.74 (m, 1H, H-1), 7.30-7.52 (m, 10H, ArH), 8.77 (s, 1H, NH). ^{13}C RMN ($CDCl_3$, 50 MHz) δ: 65.5, 66.9, 68.3, 74.9, 79.0, 81.1, 96.7 (C-1), 101.4 (C-7), 125.9, 127.9, 128.1, 128.2, 128.3, 129.1, 136.9, 137.6, 160.8. Data for **16**α. TLC: R_f(hexane-EtOAc, 4:1) = 0.36. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.60-3.88 (m, 3H), 4.00-4.12 (m, 1H, H-5), 4.19 (t, *J*= 9.5 Hz, 1H), 4.35 (dd, $J_{6,5}$= 4.7 Hz, $J_{6,6'}$= 10.2 Hz, 1H, H-6), 4.94 (dd, 2H, CH_2Ph), 5.63 (s, 1H, H-7), 6.38 (d, $J_{1,2}$= 3.7 Hz, 1H, H-1), 7.31-7.51 (m, 10H, ArH), 8.75 (s, 1H, NH).

6-*O*-[2-azido-3-*O*-benzyl-4,6-*O*-benzyliden-2-deoxy-α-D-glucopyranosyl]-2,3:4,5-di-*O* -cyclohexyliden-1-*O*-menthoxycarbonyl-*myo*-inositol (17). A mixture of 56 mg (0.11 mmol) of **16**β, 23 mg (0.04 mmol) of **6** and powdered 4Å molecular sieves in 1.1 mL of ethyl ether was stirred for 45 min at room temperature. At this time, 76 μL (0.008 mmol) of a solution of trimethylsilyl triflate in ethyl ether (0.108M) were added dropwise. The reaction mixture was stirred for 15 min., quenched with triethyl amine, diluted with CH_2Cl_2, filtrated through celite and evaporated *in vacuo*. Silica-gel column chromatography (hexane-EtOAc, 12:1) afforded

17 as a mixture of α/β (10:1) isomers and overall yield of 95%. Data for 17α: TLC: R_f (hexane-EtOAc, 6:1) = 0.38. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.77 (d, 3H, CH_3Ment), 0.88 (d, 3H, CH_3Ment), 0.92 (d, 3H, CH_3Ment), 1.04-1.12 (m, 2H, Ment), 1.27-1.74 (m, 25H, ciclohex, Ment), 1.90-2.02 (m, 1H, Ment), 2.10-2.18 (m, 1H, Ment), 3.41 (dd, $J_{2b,3b}$= 9.8 Hz, $J_{2b,1b}$= 3.9 Hz, 1H, H-2b), 3.57 (dd, $J_{5a,4a}$= 10.7 Hz, $J_{5a,6a}$= 8.8 Hz, 1H, H-5a), 3.72 (Ψt, $J_{4b,3b}$= 9.3 Hz, $J_{4b,5b}$= 9.8 Hz, 1H, H-4b), 3.74 (t, $J_{6b,6b'}$= $J_{6b,5b}$= 10.0 Hz, 1H, H-6b), 3.99 (dd, $J_{4a,5a}$= 10.7 Hz, $J_{4a,3a}$= 7.8 Hz, 1H, H-4a), 4.05 (dd, $J_{6a,5a}$= 8.8 Hz, $J_{6a,1a}$= 2.9 Hz, 1H, H-6a), 4.07 (Ψt, $J_{3b,4b}$= 9.3 Hz, $J_{3b,2b}$= 9.8 Hz, 1H, H-3b), 4.14 (dt, $J_{5b,6b'}$= 4.9 Hz, $J_{5b,6b}$= 10.2 Hz, $J_{5b,4b}$= 9.8 Hz, 1H, H-5b), 4.31 (dd, $J_{6b',6b}$= 10.0 Hz, $J_{6b',5b}$= 5.1 Hz, 1H, H-6b'), 4.39 (t, $J_{3a,2a}$= $J_{3a,4a}$= 7.3 Hz, 1H, H-3a), 4.50-4.55 (m, 1H, Ment), 4.56 (dd, $J_{2a,3a}$= 6.9 Hz, $J_{2a,1a}$= 4.1 Hz, 1H, H-2a), 4.86 (dd, 2H, CH_2Ph), 4.95 (Ψt, $J_{1a,2a}$= 3.9 Hz, $J_{1a,6a}$= 2.9 Hz, 1H, H-1a), 5.27 (d, $J_{1b,2b}$= 3.9 Hz, 1H, H-1b), 5.57 (s, 1H, H-7b), 7.25-7.35 (m, 10H, ArH). ^{13}C RMN ($CDCl_3$, 50 MHz) δ: 16.1, 20.7, 21.9, 23.2, 23.5, 23.7, 23.8, 24.9, 25.0, 26.0, 31.4, 34.0, 34.6, 36.2, 36.4, 36.6, 40.6, 47.0, 62.7, 62.8, 68.8, 73.1, 74.9, 76.2, 76.3, 76.4, 76.7, 79.0, 82.6, 97.5 (C-1b), 101.4 (C-7b), 112.1 (C*ipso* cyclohex), 113.3 (C*ipso* cyclohex), 125.9, 126.0, 127.8, 128.0, 128.2, 128.3, 128.4, 137.3, 137.9, 154.2.

6-*O*-[2-azido-3,6-di-*O*-benzyl-4-*O*-(*tert*-butyldimethylsilyl)-2-deoxy - α - D - glucopyranosyl] - 2,3:4,5 - di - *O* - cyclohexyliden - 1 - *O* - menthoxycarbonyl-*myo*-inositol (18α). A mixture of 180 mg (0.28 mmol) of **14β**, 73 mg (0.14 mmol) of **6** and powdered 4Å molecular sieves in 3 mL of ethyl ether was stirred for 45 min at room temperature. At this time, 194 μL (0.02 mmol) of a solution of trimethylsilyl triflate in ethyl ether (0.108M) were added dropwise during 45 min.. The reaction mixture was stirred for 15 min., quenched with triethyl amine, diluted with CH_2Cl_2, filtrated through celite and evaporated *in vacuo*. Silica-gel column chromatography (hexane-EtOAc) afforded **18α** and **18β** in a ratio of 9:1 and overall yield of 73%. Data for **18α**. TLC: R_f(hexane-EtOAc, 3:1) = 0.76. M.p.: 72-74°C. $[\alpha]_D$ + 47.218° (*c* 1.36, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: -0.03 (s, 3H, CH_3Si), 0.02 (s, 3H, CH_3Si), 0.76 (d, 3H, Ment), 0.86 (s, 9H, ^{t}Bu), 0.87 (d, 3H, CH_3Ment), 0.92 (d, 3H, CH_3Ment), 1.00-1.10 (m, 2H, Ment), 1.20-1.70 (m, 25H, cyclohex., Ment), 1.90-1.97 (m, 1H, Ment), 2.07-2.13 (m, 1H, Ment), 3.32 (dd, $J_{2',3'}$ = 9.8 Hz, $J_{2',1'}$ = 3.4 Hz, 1H, H-2'), 3.59 (dd, $J_{5,4}$ = 10.7 Hz, $J_{5,6}$ = 8.8 Hz, 1H, H-5), 3.64 (dd, $J_{6'b,6'a}$ = 10.9 Hz, $J_{6'b,5'}$ = 1.9 Hz, 1H, H-6'b), 3.72 (dd, $J_{6'a,6'b}$ = 10.9 Hz, $J_{6'a,5'}$ = 3.7 Hz, 1H, H-6'a), 3.76 (Ψt, $J_{3',4'}$ = $J_{3',2'}$ = 9.8 Hz, 1H, H-3'), 3.81 (Ψt, $J_{4',3'}$ = $J_{4',5'}$ = 9.8 Hz, 1H, H-4'), 3.98 (dd, $J_{4,5}$ = 10.7 Hz, $J_{4,3}$ = 7.3 Hz, 1H, H-4), 3.98-4.02 (m, 1H, H-5'), 4.14 (dd, $J_{6,5}$ = 8.8 Hz, $J_{6,1}$ = 3.4 Hz, 1H, H-6) , 4.37 (t, $J_{3,2}$ = $J_{3,4}$ = 7.3 Hz, 1H, H-3), 4.52 (dt, 1H, Ment), 4.55 (dd, 2H, CH_2Ph), 4.58 (dd, $J_{2,3}$ = 7.3 Hz, $J_{2,1}$ = 3.4 Hz, 1H, H-2), 4.82 (dd, 2H, CH_2Ph), 5.00 (t, $J_{1,2}$ = $J_{1,6}$ =

3.4 Hz, 1H, H-1), 5.31 (d, $J_{1',2'}$ = 3.4 Hz, 1H, H-1'), 7.25-7.35 (m, 10H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: -4.95, -3.65, 16.13, 18.04, 20.76, 21.92, 23.22, 23.52, 23.63, 23.83, 23.90, 24.90, 25.06, 25.92, 31.43, 34.09, 34.53, 36.33, 36.65, 40.62, 47.01, 63.46, 68.40, 70.66, 72.14, 73.26, 74.51, 76.21, 76.55, 76.71, 77.18, 79.21, 80.39, 96.80, 112.06, 113.23, 127.30, 127.42, 128.24, 138.26, 154.14. Anal. Calcd. for $C_{55}H_{81}N_3O_{12}Si$: C, 65.77; H, 8.13; N, 4.28. Found: C, 65.72; H, 8.40; N, 4.28.

6-*O*-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-2,3:4,5-di-*O*-cyclohexyliden-1-*O*-menthoxycarbonyl-*myo*-inositol (19). To a solution of 82 mg (0.08 mmol) of 18α in 0.8 mL of THF, 204 μL (0.24 mmol) of a solution 1M of tetrabutylammonium fluoride in THF were added. The reaction mixture was stirred for 45 min., quenched with water, diluted and extracted with CH_2Cl_2 and washed with brine. Silica-gel column chromatography (hexane-EtOAc, 6:1) afforded **19** in 84% yield. TLC: R_f(hexane-EtOAc, 3:1) = 0.46. M.p.: 74-76°C. $[\alpha]_D$ + 25.934° (*c* 0.99, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 0.77 (d, 3H, Ment), 0.89 (d, 3H, CH_3Ment), 0.93 (d, 3H, CH_3Ment), 0.99-1.17 (m, 2H, Ment), 1.23-1.75 (m, 25H, cyclohex., Ment), 1.87-2.05 (m, 1H, Ment), 2.07-2.20 (m, 1H, Ment), 2.75 (d, $J_{OH,4'}$ = 2.2 Hz, 1H, OH), 3.35 (dd, $J_{2',3'}$ = 9.9 Hz, $J_{2',1'}$ = 3.6 Hz, 1H, H-2'), 3.57 (dd, $J_{5,4}$ = 10.8 Hz, $J_{5,6}$ = 8.5 Hz, 1H, H-5), 3.67 (dd, $J_{6'a,6'b}$ = 10.1 Hz, $J_{6'a,5'}$ = 4.9 Hz, 1H, H-6'a), 3.77-3.86 (m, 3H), 4.00 (dd, $J_{4,5}$ = 10.8 Hz, $J_{4,3}$ = 7.4 Hz, 1H, H-4), 4.01-4.09 (m, 1H), 4.06 (dd, $J_{6,5}$ = 8.5 Hz, $J_{6,1}$ = 2.6 Hz, 1H, H-6) , 4.40 (t, $J_{3,4}$ = $J_{3,2}$ = 7.2 Hz, 1H, H-3), 4.46-4.60 (m, 2H, H-2, Ment), 4.58 (dd, 2H, CH_2Ph), 4.89 (dd, 2H, CH_2Ph), 4.99 (dd, $J_{1,2}$ = 3.9 Hz, $J_{1,6}$ = 2.6 Hz, 1H, H-1), 5.26 (d, $J_{1',2'}$ = 3.6 Hz, 1H, H-1'), 7.29-7.45 (m, 10H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 16.12, 20.73, 21.92, 23.22, 23.50, 23.65, 23.81, 23.88, 24.94, 25.04, 25.98, 31.42, 34.07, 34.55, 36.23, 36.49, 36.57, 40.61, 46.98, 62.50, 69.67, 70.50, 72.85, 73.16, 73.74, 76.19, 76.55, 76.70, 79.23, 79.72, 97.15, 112.12, 113.24, 127.66, 127.83, 127.90, 128.00, 128.44, 128.53, 137.69, 138.21, 154.16. Anal. Calcd. for $C_{49}H_{67}N_3O_{12}$: C, 66.12; H, 7.59; N, 4.72. Found: C, 65.91; H, 7.67; N, 4.52.

1,6-anhydro-3-*O*-(4-methoxibencyl)-β-D-mannopyranose (22). To a solution of 3.5 g (12.5 mmol) of 1,6-anhydro-2,3-*O*-endo-(4-methoxybencyliden)-β-D-mannopyranose[36] in 125 mL de CH_2Cl_2 at 0 °C was added slowly 40 mL (40 mmol) of a solution of DIBALH in toluene (1M). After 5 h Et_3N and MeOH were added. The crude of the reaction was diluted with EtOAc and washed with a solution of HCl (10%) and EtOAc. The organic layers were evaporated. Silica-gel column chromatography (CH_2Cl_2-MeOH, 20:1) afforded 2.8 g (79%) of **22**. TLC: R_f(CH_2Cl_2-MeOH 20:1) = 0.16. M.p.: 108-110 °C. $[\alpha]_D$: - 66.804 °(*c* 0.72, $CHCl_3$). ^1H RMN (acetone, 200 MHz) δ: 2.88 (s ancho, 1H, OH), 3.33 (d, 1H, OH), 3,56 (bt, 1H, H-6), 3.62-3.68 (m, 1H, H-2), 3.78 (s, 3H, CH_3O), 3.92 (d, 1H, H-3), 4.08 (d, 1H, H-6'), 4.27 (d, 1H, H-4), 4.40 (d, 1H, H-5), 4.56 (dd, 2H, CH_2Ph), 5.12 (bs, 1H, H-1), 6.91 (d, 2H, ArH), 7.31 (d,

2H, ArH). ^{13}C RMN ($CDCl_3$, 50 MHz) δ: 55.1, 64.5, 65.8, 69.0, 73.4, 75.7 , 78.0 , 101.8 (C-1), 129.2, 129.3, 129.5, 158.4.

1,6-anhydro-2,4-di-*O*-bencyl-3-*O*-(4-methoxybencyl)-β-D-mannopiranose (23). To a solution of 2.4 g (8.5 mmol) of **22** in 20 mL of DMF at room temperature were added 472 mg (18.7 mmol) of HNa and 1.9 mL (25.5 mmol) of BnBr. After 2 h, MeOH was added and the reaction mixture was diluted with EtOAc, washed with H_2O , dried over Na_2SO_4 and evaporated. Silica-gel column chromatography (hexano/EtOAc 3:1) afforded 3.9 g (quantitative yield) of **23**. TLC: R_f (hexane-EtOAc 2:1) = 0.31. M.p.: 68-70 °C. $[\alpha]_D$: -20.298 °(*c* 0.84, $CHCl_3$). ^1H RMN ($CDCl_3$, 200 MHz) δ: 3.48 (bt, 1H, H-4), 3.60 (dd, $J_{2,1}$= 1.7 Hz, $J_{2,3}$= 5.3 Hz, 1H, H-2), 3.66 (dd, $J_{6,6'}$= 7.0 Hz, $J_{6,5}$= 6.0 Hz, 1H, H-6), 3.74 (s, 3H, CH_3O), 3.74-3.80 (m, 1H, H-3), 4.18 (dd, $J_{6',5}$= 0.9 Hz, $J_{6',6}$= 7.1 Hz, 1H, H-6'), 4.35-4.56 (m, 7H, H-5, $3CH_2Ph$), 5.41 (bt, 1H, H-1), 6.89 (d, 2H, ArH), 7.26-7.40 (m, 12H, ArH). ^{13}C RMN ($CDCl_3$, 50 MHz) δ: 55.1, 64.8, 71.1, 71.2, 72.7, 73.9, 74.4, 76.4, 100.0 (C-1), 127.5, 127.6, 127.8, 128.2, 128.3, 129.7, 137.6, 137.9, 159.2.

1,6-di-*O*-acetyl-2,4-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-α-D-mannopyranose (24). A solution of 4.880 g (10.55 mmol) of **23** and 240 μL (1.24 mmol) of trimethylsilyltrifluoromethanesulphonate in 33 mL of acetic anhydride was stirred for 1 h at 0°C and 2 h at room temperature. The reaction mixture was diluted with EtOAc, neutralized with a saturated solution of $NaHCO_3$ in water, extracted with EtOAc and dried over Na_2SO_4. Silica-gel column chromatography afforded **24α** in 79% yield and **24β** in 3% yield. Data for **24α**: TLC: R_f(hexane-EtOAc 2:1) = 0.36. $[\alpha]_D$ + 28.098° (*c* 0.78, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 2.04 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 3.72 (Ψt, $J_{2,1} = J_{2,3}$ = 2.4 Hz, 1H, H-2), 3.81 (s, 3H, CH_3O), 3.82-4.03 (m, 3H, H-3, H-4, H-5), 4.30-4.33 (m 2H, H-6a, H-6b), 4.54 (s, 2H, CH_2Ph), 4.75 (dd, 2H, CH_2Ph), 4.77 (dd, 2H, CH_2Ph), 6.18 (d, $J_{1,2}$ = 2.1 Hz, 1H, H-1), 6.83-7.40 (m, 14H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 20.79, 20.91, 55.24, 63.17, 71.71, 72.39, 73.38, 73.80, 75.25, 78.77, 91.65, 113.80, 113.95, 127.78, 127.86, 128.11, 128.35, 128.42, 129.37, 130.04, 137.78, 138.00. Anal. Calcd. for $C_{32}H_{36}O_9$: C, 68.08; H, 6.43. Found: C, 68.29; H, 6.12. Data for **24β**: TLC: R_f (hexane-EtOAc, 2:1) = 0.31. $[\alpha]_D$ + 0.740° (*c* 4.22, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 2.05 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 3.55-3.66 (m, 1H, H-5), 3.63 (dd, $J_{3,2}$ = 2.8 Hz, $J_{3,4}$ = 9.1 Hz, 1H, H-3), 3.82 (s, 3H, CH_3O), 3.87-3.96 (m, 2H, H-2, H-4), 4.30-4.35 (m 2H, H-6a, H-6b), 4.57 (dd, 2H, CH_2Ph), 4.76 (dd, 2H, CH_2Ph), 4.87 (s, 2H, CH_2Ph), 5.60 (d, $J_{1,2}$ = 0.9 Hz, 1H, H-1), 6.84-7.48 (m, 14H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.10, 20.80, 20.93, 55.16, 60.27, 63.25, 71.78, 73.37, 73.81, 74.07, 74.36, 75.03, 81.75, 92.92, 113.81, 127.61, 127.79, 128.00, 128.10, 128.14, 128.35, 129.24, 129.76, 137.83, 138.16, 159.28, 168.8, 170.74. Anal. Calcd. for $C_{32}H_{36}O_9$: C, 68.08; H, 6.43. Found: C, 67.84; H, 6.71.

1,6-di-*O*-acetyl-2,4-di-*O*-benzyl-α-D-mannopyranose (25) .To a solution of 100 mg (0.18 mmol) of **24** in 1.5 mL of CH_2Cl_2 was added 50 μL of trifluoroacetic acid in 2 mL of CH_2Cl_2. The reaction mixture was stirred for 3 h at room temperature, neutralized with a saturated solution of $NaHCO_3$ in water, extracted with CH_2Cl_2 and dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **25** in 98% yield. TLC: R_f(hexane-EtOAc, 2:1) = 0.24. $[\alpha]_D$ + 29.671° (*c* 1.52, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 2.08 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 2.43 (d, $J_{OH,3}$ = 9.7 Hz, 1H, OH), 3.68 (t, $J_{4,3} = J_{4,5}$ = 9.6 Hz, 1H, H-4), 3.74 (dd, $J_{2,3}$ = 3.8 Hz, $J_{2,1}$ = 1.8 Hz, 1H, H-2), 3.88 (ddd, $J_{5,4}$ = 9.8 Hz, $J_{5,6a}$ = 4.6 Hz, $J_{5,6b}$ = 2.3 Hz, 1H, H-5), 4.01 (dt, $J_{3,4} = J_{3,OH}$ = 9.6 Hz, $J_{3,2}$ = 3.8 Hz, 1H, H-3), 4.30 (dd, $J_{6a,6b}$ = 12.0 Hz, $J_{6a,5}$ = 4.6 Hz, 1H, H-6a), 4.38 (dd, $J_{6b,6a}$ = 12.0 Hz, $J_{6b,5}$ = 2.3 Hz, 1H, H-6b), 4.71 (dd, 2H, CH_2Ph), 4.78 (dd, 2H, CH_2Ph), 6.27 (d, $J_{1,2}$ = 1.8 Hz, 1H, H-1), 7.30-7.41 (m, 10H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 20.80, 20.91, 63.14, 71.47, 71.62, 72.67, 75.05, 75.63, 76.78, 90.73, 127.98, 128.11, 128.25, 128.48, 128.64, 128.64, 137.15, 137.91, 168.91, 170.74. Anal. Calcd. for $C_{24}H_{28}O_8$: C, 64.86; H, 6.35. Found: C, 64.44; H, 6.38.

1,6-di-*O*-acetyl-2,4-di-*O*-benzyl-3-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranose (26) .To a solution of 1.400 g (3.15 mmol) of **25**, 170 mg (1.39 mmol) of 4-dimethylaminopyridine and 857 mg (12.60 mmol) of imidazole in 5 mL of DMF, were added 1.64 mL (6.30 mmol) of *tert*-butyldiphenylsilyl chloride. The reaction mixture was stirred for 17 h at room temperature, diluted with ethyl ether, washed with water and brine and dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 10:1, 4:1) afforded **26** in 89% yield. TLC: R_f(hexane-EtOAc, 2:1) = 0.55. M.p. = 107-109°C $[\alpha]_D$ + 44.830° (*c* 1.13, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 1.14 (s, 9H, ^{t}Bu), 1.89 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 3.03 (bs, 1H, H-2), 3.85 (ddd, $J_{5,4}$ = 9.6 Hz, $J_{5,6a}$ = 4.3 Hz, $J_{5,6b}$ = 2.2 Hz, 1H, H-5), 4.07 (bt, $J_{4,3} = J_{4,5}$ = 9.2 Hz, 1H, H-4), 4.22-4.37 (m, 2H, H-6a, H-6b), 4.32 (dd, $J_{3,4}$ = 8.9 Hz, $J_{3,2}$ = 3.1 Hz, 1H, H-3), 4.42 (dd, 2H, CH_2Ph), 4.58-4.72 (bm, 1H, CH_2Ph), 4.99-5.12 (bm, 1H, CH_2Ph), 5.95 (d, $J_{1,2}$ = 2.1 Hz, 1H, H-1), 7.24-7.77 (m, 20H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.32, 20.81, 27.06, 63.22, 72.05, 72.69, 72.99, 75.23, 76.36, 77.05, 91.30, 127.21, 127.31, 127.46, 127.66, 127.72, 127.77, 128.00, 128.18, 128.38, 129.83, 130.03, 133.12, 134.13, 135.92, 136.08, 137.86, 138.16. Anal. Calcd. for $C_{40}H_{46}O_8Si$: C, 70.36; H, 6.79. Found: C, 70.61; H, 6.77.

Phenyl 6-*O*-acetyl-2,4-di-*O*-benzyl-3-*O*-(*tert*-butyldiphenylsilyl)-1-thio-α-D-mannopyranoside (27) .To a solution of 1.800 g (2.64 mmol) of **26** in 26 mL of CH_2Cl_2 at room temperature were added 592 μL (4.80 mmol) of thiophenol and 1.32 mL (10.5 mmol) of borontrifluoride diethyl etherate. The reaction mixture was stirred for 30 min., quenched with a saturated solution of $NaHCO_3$ in water and the organic layer dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc,

10:1) afforded 27α and 27β in a ratio of 8:1 and overall yield of 97%. Data for 27α. TLC: R_f(hexane-EtOAc, 5:1) = 0.40. $[\alpha]_D$ + 126.143° (*c* 1.21, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 1.17 (s, 9H, ^{t}Bu), 2.02 (s, 3H, CH_3CO), 3.29 (m, 1H, H-2), 3.97-4.07 (m, 1H, H-4), 4.21-4.37 (m, 5H, H-5, H-6a, H-6b, CH_2Ph), 4.37 (dd, $J_{3,4}$ = 8.8 Hz, $J_{3,2}$ = 2.8 Hz, 1H, H-3), 4.59-4.68 (bm, 1H, CH_2Ph), 4.97-5.18 (bm, 1H, CH_2Ph), 5.26 (d, $J_{1,2}$ = 1.5 Hz, 1H, H-1), 7.21-7.84 (m, 25H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.32, 20.79, 27.17, 29.67, 63.57, 71.03, 71.83, 74.04, 74.08, 75.25, 76.13, 77.19, 79.59, 85.23, 127.28, 127.36, 127.42, 127.27, 127.76, 127.89, 127.97, 128.17, 128.26, 128.36, 128.81, 129.82, 129.96, 131.62, 133.11, 134.31, 136.08, 138.00, 138.26, 170.72. Anal. Calcd. for $C_{44}H_{48}O_6SSi$: C, 72.10; H, 6.60; S, 4.37. Found: C, 72.31; H, 6.35; S, 4.12.

Phenyl 2,4-di-*O*-benzyl-3-*O*-(*tert*-butyldiphenylsilyl)-1-thio-α-D-mannopyranoside (28) .To a solution of 100 mg (0.14 mmol) of 27α in 2 mL of methanol was added 0.4 mL of sodium methoxide in methanol (1M). The reaction mixture was stirred for 1 h at room temperature, neutralized with Amberlite IR-120, filtrated and evaporated. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded 28 in quantitative yield. TLC: R_f(hexane-EtOAc, 3:1) = 0.46. M.p. = 46-48°C. $[\alpha]_D$ + 131.182° (*c* 1.17, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 1.16 (s, 9H, ^{t}Bu), 3.32 (m, 1H, H-2), 3.77-3.81 (m, 2H), 4.05-4.08 (m, 2H, H-4), 4.32 (dd, 2H, CH_2Ph), 4.38 (dd, $J_{3,4}$ = 8.8 Hz, $J_{3,2}$ = 3.1 Hz, 1H, H-3), 4.62-4.77 (bm, 1H, CH_2Ph), 4.97-5.10 (bm, 1H, CH_2Ph), 5.20 (d, $J_{1,2}$ = 1.7 Hz, 1H, H-1), 7.21-7.84 (m, 25H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.31, 27.16, 62.21, 72.24, 73.34, 73.89, 75.16, 76.02, 127.39, 127.41, 127.63, 127.71, 127.88, 128.23, 128.33, 128.90, 129.77, 129.92, 131.66, 133.21, 134.46, 136.07, 138.27. Anal. Calcd. for $C_{42}H_{46}O_5SSi$: C, 73.10; H, 6.71; S, 4.64. Found: C, 73.12; H, 6.43; S, 4.37.

3 - *O* - benzyl - 4,6 - *O* - benzylidene - 2 - deoxy - 2 - phthalimido - β - D - glucopyranosyl fluoride (29). To a solution of 100 mg (0.17 mmol) of phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[46] in 1.7 mL of CH_2Cl_2 at -15°C, 68 μL (0.52 mmol) of diethylaminosulfur triflluoride were added dropwise and then 46 mg (0.26 mmol) of N-bromosuccinimide. The reaction mixture was stirred for 4 h 30 min., quenched with a saturated solution of $NaHCO_3$ in water/ice, extracted with CH_2Cl_2 and dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 4:1) afforded **29** in quantitative yield. TLC: R_f(toluene-EtOAc, 10:1) = 0.56. M.p.: 173-175°C. $[\alpha]_D$ + 62.003° (*c* 0.99, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 3.60-3.78 (m, 1H), 3.84-3.96 (m, 2H), 4.24-4.52 (m, 3H), 4.65 (dd, 2H, CH_2Ph), 5.64 (s, 1H, H-7), 5.90 (dd, 1H, $J_{F,1}$ = 53.4 Hz, $J_{1,2}$ = 7.6 Hz, H-1), 6.84-7.80 (m, 14H, ArH). ^{13}C NMR (50

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[46] Ogawa, T.; Nakabayashi, S.; Kasajima, K. *Carbohyd. Res.* **1981**, 95, 308-312.

MHz, $CDCl_3$) δ: 41.98, 55.57, 55.98, 65.72, 65.82, 68.36, 73.74, 73.93, 74.15, 82.36, 101.48, 102.93, 107.22, 123.49, 126.04, 127.52, 128.07, 128.30, 129.12, 131.51, 134.04, 137.04, 137.62. Anal. Calcd. for $C_{28}H_{24}FNO_6$: C, 68.70; H, 4.94; N, 2.86. Found: C, 68.48; H, 5.10; N, 2.85.

Phenyl *O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→6)-2,4-di-*O*-benzyl-3-*O*-(*tert*-butyldiphenylsilyl)-1-thio-α-D-mannopyranoside (30). A mixture of 166 mg (0.24 mmol) of **28**, 323 mg (1.08 mmol) of zirconocene dichloride, 562 mg (2.16 mmol) of silver triflate and powdered 4Å molecular sieves in 5 mL of CH_2Cl_2 in darkness was stirred for 30 min at room temperature. At this time, the reaction mixture was cooled to -40°C and 176 mg (0.36 mmol) of **29** in 2.3 mL of CH_2Cl_2 were added dropwise during 1 h 20 min.. After one night at -30°C, the mixture was quenched with a saturated solution of $NaHCO_3$ in water, diluted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, concentrated and chromatographed (ether/cyclohexane, 1:2) to yield 82% of **30**. TLC: R_f(hexane-EtOAc, 3:1) = 0.36. M.p.: 82-85°C. $[\alpha]_D$ + 89.610° (*c* 0.95, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.99 (s, 9H, ^{t}Bu), 3.15 (bs, 1H, H-2), 3.61 (dt, $J_{5',4'} = J_{5',6'a}$ = 9.8 Hz, $J_{5',6'b}$ = 4.9 Hz, 1H, H-5'), 3.70-3.79 (m, 4H), 3.99-4.08 (m, 3H), 4.17-4.25 (m, 3H), 4.30-4.36 (m, 2H), 4.41-4.54 (m, 2H), 4.63 (dd, 2H, CH_2Ph), 5.13 (bs, 1H, H-1), 5.29 (d, $J_{1',2'}$ = 8.3 Hz, 1H, H-1'), 5.56 (s, 1H, H-7'), 7.18-7.66 (m, 39H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.21, 27.09, 55.57, 66.12, 68.48, 68.70, 71.57, 72.17, 73.72, 74.03, 74.63, 75.91, 76.66, 76.81, 77.20, 77.42, 78.00, 78:15, 79.58, 82.97, 85.27, 99.00, 101.30, 123.21, 126.07, 126.94, 127.18, 127.31, 127.51, 127.60, 127.99, 128.19, 128.27, 128.80, 128.97, 129.63, 129.84, 131.13, 131.65, 133.17, 133.59, 134.35, 134.89, 136.03, 137.42, 138.00, 138.31. Anal. Calcd. for $C_{70}H_{69}NO_{11}SSi$: C, 72.45; H, 5.99; N, 1.21; S, 2.76. Found: C, 72.21; H, 6.10; N, 1.29; S, 2.57.

***O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→6)-2,4-di-*O*-benzyl-3-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranose (31).** To a solution of 105 mg (0.09 mmol) of **30** in 1.8 mL of acetone in darkness at -15°C, 24 mg (0.14 mmol) of N-bromosuccinimide were added. Ten minutes later, the reaction mixture was quenched with a saturated solution of $NaHCO_3$ in water, diluted and extracted with EtOAc, washed with brine and dried. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **31** in 94% yield. TLC: R_f(hexane-EtOAc, 3:1) = 0.15. M.p. = 74-76°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.04 (s, 9H, ^{t}Bu), 2.60 (d, $J_{OH,1}$ = 2.5 Hz, 1H, OH), 3.03 (Ψt, $J_{2,1} = J_{2,3}$ = 2.8 Hz, 1H, H-2), 3.41-3.90 (m, 7H), 4.11-4.80 (m, 12H), 5.55 (d, $J_{1',2'}$ = 8.3 Hz, 1H, H-1'), 5.60 (s, 1H, H-7'), 7.10-7.71 (m, 34H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.22, 27.18, 55.88, 66.13, 68.19, 68.85, 72.51, 72.79, 73.21, 74.01, 74.36, 74.57, 74.65, 75.79, 76.67, 77.20, 77.40, 78.19, 78.32, 83.26, 92.32, 98.86, 101.38, 123.24,

126.09, 127.34, 127.48, 127.62, 127.68, 127.80, 128.19, 128.01, 128.15, 128.26, 128.97, 129.56, 129.69, 129.83, 131.56, 131.63, 133.53, 133.76, 133.91, 134.37, 136.12, 137.44, 137.80, 137.98, 138.59. Anal. Calcd. for $C_{64}H_{65}NO_{12}Si$: C, 71.96; H, 6.13; N, 1.31. Found: C, 71.71; H, 5.85; N, 1.37.

***O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→6)-2,4-di-*O*-benzyl-3-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranosyl trichloracetimidate (32).** To a solution of 53 mg (0.05 mmol) of **31** in 0.25 mL of CH_2Cl_2 at room temperature, were added 50 μL (0.50 mmol) of trichloracetonitrile and 7 mg (0.05 mmol) of activate potasium carbonate. After 4 h, the reaction mixture was diluted with CH_2Cl_2, filtrated through celite and evaporated. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **32α** and **32β** in a ratio of 13:1 and overall yield of 88%. Data for **32α**: TLC: R_f(hexane-EtOAc, 3:1) = 0.36. M.p. = 76-78°C. $[\alpha]_D$ +34.180° (*c* 0.61, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ: 1.02 (s, 9H, ^{t}Bu), 3.21 (m, 1H, H-2), 3.56-3.87 (m, 6H), 4.04-4.62 (m, 9H), 4.64 (dd, 2H, CH_2Ph), 5.28 (d, $J_{1',2'}$ = 8.2 Hz, 1H, H-1'), 5.60 (s, 1H, H-7'), 5.74 (m, 1H, H-1), 7.10-7.65 (m, 34H, ArH), 8.09 (s, 1H, NH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.23, 27.13, 55.69, 66.09, 68.84, 72.19, 72.96, 73.87, 74.02, 74.76, 75.54, 76.23, 83.04, 95.81, 99.22, 101.32, 123.19, 126.08, 127.23, 127.29, 127.52, 127.67, 127.97, 128.19, 128.25, 128.96, 129.59, 129.80, 131.72, 133.08, 133.51, 134.27, 136.02, 137.44, 137.85, 138.04, 138.33, 159.80, 167.54. Anal. Calcd. for $C_{66}H_{65}Cl_3N_2O_{12}Si$: C, 65.37; H, 5.40; N, 2.31. Found: C, 65.10; H, 5.10; N, 2.07.

Phenyl 6-*O*-acetyl-2-*O* -benzyl-3,4-*O* -isopropylidene-1-thio-β-D-galactopyranoside (35). To a solution of 193 mg (0.48 mmol) of phenyl 2- *O*-benzyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside[45] in 0.77 mL of pyridine and DMAP in catalitic amount at 0°C, was added dropwise 0.11 mL (1.20 mmol) of acetic anhydride. The reaction mixture was stirred for 5 min. at 0°C and 90 min. at room temperature. After this time, the reaction was evaporated. Silica-gel column chromatography (hexane-EtOAc, 4:1) afforded **35** in quantitative yield. TLC: R_f(hexane-EtOAc, 3:1) = 0.35. $[\alpha]_D$ +9.209° (*c* 1.10, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.35 (s, 3H, ^{i}Pr), 1.41 (s, 3H, ^{i}Pr), 2.06 (s, 3H, Ac), 3.54 (dd, $J_{2,3}$ = 6.2 Hz, $J_{2,1}$ = 9.4 Hz, 1H, H-2), 3.94 (dt, $J_{5,4}$ = 2.1 Hz, $J_{5,6}$ = 6.0 Hz, 1H, H-5), 4.19 (dd, $J_{4,5}$ = 2.0 Hz, $J_{4,3}$ = 5.8 Hz, 1H, H-4), 4.28 (t, $J_{3,4} = J_{3,2}$ = 6.0 Hz, 1H, H-3), 4.34 (d, $J_{6,5}$ = 6.1 Hz, 2H, H-6a, H-6b), 4.63 (d, $J_{1,2}$ = 9.4 Hz, 1H, H-1), 4.76 (dd, 2H, CH_2Ph), 7.25-7.57 (m, 10H, ArH). ^{13}C NMR (50 MHz, C_6D_6) δ: 20.33, 26.29, 27.73, 63.92, 73.52, 73.89, 74.42, 78.81, 79.89, 86.38, 110.27, 127.52, 127.83, 128.28, 128.92, 129.62, 130.02, 130.24, 132.58, 134.82, 138.73, 169.87. Anal. Calcd. for $C_{24}H_{28}O_6S$: C, 64.85; H, 6.35; S, 7.21. Found: C, 65.17; H, 6.08; S, 7.25.

6-*O*-acetyl-2-*O* -benzyl-3,4-*O* -isopropylidene-D-galactopyranose (36). A solution of 115 mg (0.259 mmol) of **35** in 5 mL of acetone was cooled to

-15 C. Then 60 mg (0.336 mmol) of N-bromosuccinimide and 5 μL (0.284 mmol) of water were added. After 10 minutes the reaction mixture was quenched with a saturated solution of $NaHCO_3$ in water, diluted and extracted with EtOAc, washed with brine and dried over Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **36** in 94% yield. TLC: R_f(hexane-EtOAc, 2:1) = 0.17. M.p. = 122-124°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.34 (s, 3H, ^{i}Prα+β), 1.43 (s, 3H, ^{i}Prα), 1.46 (s, 3H, ^{i}Prβ), 2.09 (s, 3H, Acα), 2.10 (s, 3H, Acβ), 3.32 (d, $J_{OH,1}$ = 6.4 Hz, 1H, OH), 3.52 (t, $J_{2,1} = J_{2,3}$ = 5.5 Hz, 1H, H-2β), 3.67 (dd, $J_{2,1}$ = 3.8 Hz, $J_{2,3}$ = 5.7 Hz, 1H, H-2α), 4.08 (ddd, J = 2.1 Hz, J = 4.8 Hz, J = 7.0 Hz, 1H, H-5β), (dt, J = 4.3 Hz, J = 1.6 Hz, 1H, H-5α), 4.21-4.39 (m, 4H, H-3β, H-4, H-6a, H-6b), 4.45 (t, J = 6.0 Hz, 1H, H-3α), 4.75 (dd, 2H, CH_2Ph), 4.85 (dd, $J_{1,OH}$ = 5.4 Hz, $J_{1,2}$ = 7.9 Hz, 1H, H-1β), 5.22 (dd, $J_{1,2}$ = 3.8 Hz, $J_{3,OH}$ = 6.3 Hz, 1H, H-1α), 7.29-7.39 (m, 5H, ArH). ^{13}C NMR (50 MHz, C_6D_6) δ: 13.38, 20.90, 25.58, 25.75, 27.15, 27.24, 63.74, 63.89, 66.85, 70.14, 72.96, 73.17, 73.41, 74.07, 75.36, 78.46, 90.57, 95.66, 109.95, 110.33, 127.92, 128.03, 128.18, 128.46, 128.58, 137.41, 137.70, 170.84. Anal. Calcd. for $C_{18}H_{24}O_7$: C, 61.36; H, 6.86. Found: C, 61.14; H, 6.66.

6-*O*-acetyl-2-*O* -benzyl-3,4-*O* -isopropylidene-D-galactopyranosyl trichloracetimidate (37). To a solution of 81 mg (0.230 mmol) of **36** in 1.2 mL of CH_2Cl_2 at room temperature, were added 230.5 μL (2.30 mmol) of trichloracetonitrile and 76 mg (0.552 mmol) of activated potasium carbonate. After 5 h 45 min. the reaction mixture was diluted with CH_2Cl_2, filtrated through celite and evaporated. Silica-gel column chromatography (hexane-EtOAc, 6:1) afforded **37α** and **37β** in a ratio of 3:8 and overall yield of 92%. Data for **37β**: TLC: R_f(hexane-AcOEt, 3:1) = 0.17. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.35 (s, 3H, ^{i}Pr), 1.42 (s, 3H, ^{i}Pr), 2.08 (s, 3H, Ac), 3.70 (dd, $J_{2,3}$ = 6.3 Hz, $J_{2,1}$ = 7.3 Hz, 1H, H-2), 4.12-4.17 (m, 1H, H-5), 4.23 (dd, $J_{4,5}$ = 2.2 Hz, $J_{4,3}$ = 5.9 Hz, 1H, H-4), 4.30-4.38 (m, 3H, H-3, H-6a, H-6b), 4.34 (dd, 2H, CH_2Ph), 5.76 (d, $J_{1,2}$ = 7.6 Hz, 1H, H-1), 7.28-7.40 (m, 5H, ArH), 8.66 (s, 1H, NH). Data for **37α**: TLC: R_f(hexane-AcOEt, 3:1) = 0.37. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.35 (s, 3H, ^{i}Pr), 1.41 (s, 3H, ^{i}Pr), 2.05 (s, 3H, Ac), 3.81 (dd, $J_{2,3}$ = 6.8 Hz, $J_{2,1}$ = 3.5 Hz, 1H, H-2), 4.23-4.49 (m, 5H, H-3, H-4, H-5, H-6a, H-6b), 4.76 (dd, 2H, CH_2Ph), 6.43 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 7.28-7.37 (m, 5H, ArH), 8.64 (s, 1H, NH).

Phenyl *O*- (6- *O*- acetyl- 2-*O* -benzyl- 3,4- *O*-isopropylidene- α -D - galactopyranosyl)- (1→6)- 2- *O* - benzyl- 3,4- *O* -isopropyliden -1 -thio - β- D -galactopyranoside (38). A mixture of 64 mg (0.129 mmol) of **37β**, 45 mg (0.112 mmol) of **34** and activated powdered 4Å molecular sieves in 2.1 mL of ethyl ether was stirred for 90 min. at room temperature. At this time, 155 μL (0.017 mmol) of a solution of trimethylsilyl triflate in ethyl ether (0.108M) were added. The reaction mixture was stirred for 45 min., quenched with triethyl amine, diluted with CH_2Cl_2, filtrated

through celite and evaporated *in vacuo*. Silica-gel column chromatography (hexane-EtOAc) afforded **38α** and **38β** in a ratio of 6:1 and overall yield of 86%. Data for **38α**. TLC: R_f(hexane-EtOAc, 2:1) = 0.42. M.p.: 45-47°C. $[\alpha]_D$ + 48.273° (*c* 0.88, $CHCl_3$). ^1H NMR (300 MHz, C_6D_6, 30°C) δ: 1.24 (s, 3H, ^{i}Pr), 1.26 (s, 3H, ^{i}Pr), 1.35 (s, 3H, ^{i}Pr), 1.41 (s, 3H, ^{i}Pr), 1.77 (s, 3H, Ac), 3.50-3.59 (m, 2H, H-5, H-6b), 3.69 (dd, $J_{2,3}$ = 6.3 Hz, $J_{2,1}$ = 9.5 Hz, 1H, H-2), 3.71 (dd, $J_{2',3'}$ = 7.7 Hz, $J_{2',1'}$ = 3.5 Hz, 1H, H-2'), 3.76 (dd, $J_{4,5}$ = 1.9 Hz, $J_{4,3}$ = 5.7 Hz, 1H, H-4), 3.85 (dd, $J_{4',5'}$ = 2.6 Hz, $J_{4',3'}$ = 5.5 Hz, 1H, H-4'), 4.05 (t, $J_{3,4} = J_{3,2}$ = 6.0 Hz, 1H, H-3), 4.19 (dd, $J_{6a,6b}$ = 9.5 Hz, $J_{6a,5}$ = 7.0 Hz, 1H, H-6a), 4.44 (ddd, $J_{5',4'}$ = 2.6 Hz, $J_{5',6'a}$ = 8.0 Hz, $J_{5',6'b}$ = 4.1 Hz, 1H, H-5'), 4.46-4.63 (m, 2H, H-6'a, H-6'b), 4.56 (dd, $J_{3',4'}$ = 5.5 Hz, $J_{3',2'}$ = 7.7 Hz, 1H, H-3'), 4.68 (d, $J_{1,2}$ = 9.5 Hz, 1H, H-1), 4.75 (dd, 2H, CH_2Ph), 4.84 (dd, 2H, CH_2Ph), 4.96 (d, $J_{1',2'}$ = 3.5 Hz, 1H, H-1'), 7.01-7.64 (m, 15H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 20.82, 26.29, 27.72, 27.96, 63.35, 65.56, 66.90, 72.43, 73.37, 73.73, 74.90, 75.85, 76.18, 78.00, 79.59, 84.74, 96.68, 109.15, 110.14, 126.58, 127.76, 127.89, 128.19, 128.25, 128.32, 128.76, 129.76, 134.57, 137.65, 138.06, 170.59. Anal. Calcd. for $C_{40}H_{48}O_{11}S$: C, 65.20; H, 6.57; S, 4.35. Found: C, 65.05; H, 6.54; N, 4.14. Data for **38β**. TLC: R_f(hexane-AcOEt, 2:1) = 0.33. ^1H NMR (300 MHz, C_6D_6, 30°C) δ: 1.33 (s, 3H, ^{i}Pr), 1.35 (s, 3H, ^{i}Pr), 1.37 (s, 3H, ^{i}Pr), 1.42 (s, 3H, ^{i}Pr), 2.09 (s, 3H, Ac), 3.39 (dd, $J_{2',3'}$ = 6.4 Hz, $J_{2',1'}$ = 7.8 Hz, 1H, H-2'), 3.55 (dd, $J_{2,3}$ = 6.1 Hz, $J_{2,1}$ = 9.2 Hz, 1H, H-2), 3.88 (dt, $J_{5',6'a} = J_{5',6'b}$ = 6.1 Hz, $J_{5',4'}$ = 2.0 Hz, 1H, H-5'), 3.94-4.21 (m, 4H), 4.10 (dd, $J_{4',5'}$ = 2.0 Hz, $J_{4',3'}$ = 5.7 Hz, 1H, H-4'), 4.14 (t, $J_{3',4'} = J_{3',2'}$ = 6.0 Hz, 1H, H-3'), 4.28 (t, $J_{3,4} = J_{3,2}$ = 5.9 Hz, 1H, H-3), 4.33 (d, $J_{6'a,5} = J_{6'b,5}$ = 6.1 Hz, 2H, H-6'a, H-6'b), 4.42 (d, $J_{1',2'}$ = 7.8 Hz, 1H, H-1'), 4.72 (d, $J_{1,2}$ = 9.2 Hz, 1H, H-1), 4.66-4.84 (m, 4H, $2CH_2Ph$), 7.16-7.53 (m, 15H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 20.85, 26.30, 27.66, 63.47, 69.09, 70.70, 73.39, 73.44, 73.87, 75.81, 77.96, 78.72, 79.16, 79.42, 86.00, 103.10, 110.12, 110.21, 127.01, 127.46, 127.73, 128.19, 128.28, 128.84, 131.12, 137.83, 138.22, 170.70.

***O*- (6- *O*- acetyl- 2- *O*-benzyl- 3,4- *O*-isopropylidene- α -D - galactopyranosyl)- (1→ 6)- 2- *O* - benzyl- 3,4- *O* -isopropyliden - D - galactopyranose (39).** To a solution of 233 mg (0.316 mmol) of **38α** in 6.5 mL of acetone at -15°C, were added 73 mg (0.411 mmol) of N-bromosuccinimide and 6.3 μL (0.348 mmol) of water. In 5 min. the reaction was finished and quenched with a saturated solution of sodium bicarbonate in water. The mixture was diluted and extracted with EtOAc and washed with brine. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **39** in quantitative yield. TLC: R_f(hexane- EtOAc, 2:1) = 0.12. ^1H NMR (200 MHz, $CDCl_3$) δ: 1.30 (s, 3H, ^{i}Pr), 1.33 (s, 3H, ^{i}Pr), 1.38 (s, 3H, ^{i}Pr), 1.40 (s, 3H, ^{i}Pr), 2.05 (s, 3H, Acα), 2.06 (s, 3H, Acβ), 2.74 (s, 1H, OH), 3.37 (t, $J_{2,3} = J_{2,1}$ = 6.3 Hz, 1H, H-2β), 3.52 (dd, $J_{2',3'}$ = 7.7 Hz, $J_{2',1'}$ = 3.6 Hz, 1H, H-2'), 3.63 (dd, *J*

$J_{2,3}$ = 5.7 Hz, $J_{2,1}$ = 3.7 Hz, 1H, H-2α), 3.68-3.92 (m, 2H), 4.00-4.46 (m, 8H), 4.66-4.84 (m, 6H), 4.82 (m, 1H, H-1α), 7.26-7.38 (m, 10H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 20.85, 21.03, 25.78, 25.89, 26.34, 27.31, 27.41, 28.02, 63.71, 63.87, 65.38, 65.56, 67.34, 67.60, 67.88, 71.40, 72.26, 72.35, 72.97, 73.07, 73.50, 73.68, 74.20, 75.41, 75.88, 75.97, 78.31, 78.58, 79.22, 79.31, 79.54, 90.54, 96.20, 97.08, 97.28, 109.37, 109.41, 109.57, 109.93, 127.72, 127.81, 127.86, 127.97, 128.01, 128.14, 128.33, 128.50, 137.59, 137.99, 138.16, 138.23, 170.01. 171.75.

***O*- (6- *O*- acetyl- 2- *O*-benzyl- 3,4- *O*-isopropylidene- α -D - galactopyranosyl)- (1→ 6)- 2- *O* - benzyl- 3,4- *O* -isopropyliden - D -galactopyranosyl trichloracetimidate (40).** To a solution of 185 mg (0.287 mmol) of **39** in 1.5 mL of CH_2Cl_2, were added 288 μL (2.870 mmol) of trichloroacetonitrile and 80 mg (0.574 mmol) of activated potasium carbonate. The reaction mixture was stirred for 2 hours, diluted with CH_2Cl_2 and filtrated through celite. The solvent was evaporated and after a silica-gel column chromatography (hexane-EtOAc, 4:1), **40α** and **40β** (2:3) were obtain with 80% of overall yield. Data for **40α**. TLC: R_f(hexane-EtOAc, 2:1) = 0.49. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.31 (s, 3H, ^{i}Pr), 1.32 (s, 3H, ^{i}Pr), 1.37 (s, 3H, ^{i}Pr), 1.39 (s, 3H, ^{i}Pr), 2.04 (s, 3H, Ac), 3.51 (dd, $J_{2',3'}$ = 7.7 Hz, $J_{2',1'}$ = 3.4 Hz, 1H, H-2'), 3.72 (dd, $J_{6a,6b}$ = 10.5 Hz, $J_{6a,5}$ = 5.2 Hz, 1H, H-6a), 3.80 (dd, $J_{2,3}$ = 6.6 Hz, $J_{2,1}$ = 3.6 Hz, 1H, H-2), 3.88 (dd, $J_{6b,6a}$ = 10.5 Hz, $J_{6b,5}$ = 7.1 Hz, 1H, H-6b), 4.14 (dd, J = 2.5 Hz, J = 5.6 Hz, 1H), 4.17-4.50 (m, 5H, H-3, H-3', H-5, H-5'), 4.30 (d, $J_{5',6'}$ = 8.4 Hz, 2H, H-6'a, H-6'b), 4.65-4.85 (m, 4H, 2CH_2Ph), 4.72 (d, $J_{1',2'}$ = 3.5 Hz, 1H, H-1'), 6.38 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 7.25-7.38 (m, 10H, ArH), 8.57 (s, 1H, NH). Data for **40β**. TLC: R_f(hexane-AcOEt, 2:1) = 0.27. $[\alpha]_D$+66.848° (*c* 0.92, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.32 (s, 6H, ^{i}Pr), 1.38 (s, 3H, ^{i}Pr), 1.39 (s, 3H, ^{i}Pr), 2.05 (s, 3H, Ac), 3.53 (dd, $J_{2',3'}$ = 7.5 Hz, $J_{2',1'}$ = 3.4 Hz, 1H, H-2'), 3.67 (dd, $J_{2,3}$ = 6.1 Hz, $J_{2,1}$ = 7.7 Hz, 1H, H-2), 3.71 (dd, $J_{6a,6b}$ = 10.0 Hz, $J_{6a,5}$ = 5.6 Hz, 1H, H-6a), 3.94 (dd, $J_{6b,6a}$ = 10.3 Hz, $J_{6b,5}$ = 6.8 Hz, 1H, H-6b), 4.08-4.38 (m, 8H, H-3, H-3', H-4, H4', H-5, H-5', H-6'a, H-6'b), 4.74 (dd, 2H, CH_2Ph), 4.83 (dd, 2H, CH_2Ph), 4.85 (d, $J_{1',2'}$ = 3.4 Hz, 1H, H-1'), 5.72 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 7.26-7.41 (m, 10H, ArH), 8.63 (s, 1H, NH). Anal. Calcd. for $C_{36}H_{44}Cl_3NO_{12}$: C, 54.80; H, 5.62; N, 1.77. Found: C, 55.00; H, 5.76; N, 1.81.

***O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→6)-*O*-[2,4-di-*O*-benzyl-3-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranosyl]-(1→4)-*O*-[6-*O*-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)]-2,3:4,5-di-*O*-cyclohexyliden-1-*O*-menthoxycarbonyl -*myo*-inositol (41).** A mixture of 35 mg (0.03 mmol) of **32**, 17 mg (0.02 mmol) of **19** and powdered 4Å molecular sieves in 0.4 mL of ethyl ether was stirred for 45 min at room temmperature. Al this time, 41 μL (0.004 mmol) of a

solution of trimethylsilyl triflate in ethyl ether (0.108M) were added dropwise. The reaction mixture was stirred for 2 h 30 min., quenched with triethyl amine, diluted with CH_2Cl_2, filtrated through celite, evaporated *in vacuo* and chromatographed (hexane-EtOAc, 3:1 (3)) to yield 81% of **41**. TLC: R_f(hexane-EtOAc, 3:1) = 0.46. M.p. = 104-107°C. $[\alpha]_D$ + 40.598° (*c* 1.31, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.69 (d, 3H, Ment), 0.81 (d, 3H, CH_3Ment), 0.83 (d, 3H, CH_3Ment), 0.90 (s, 9H, ^{t}Bu), 0.91-1.01 (m, 2H, Ment), 1.08-1.15 (m, 1H, Ment), 1.16-1.23 (m, 1H, Ment), 1.30-1.70 (m, 23H, cyclohex., 3 Ment), 1.85-1.92 (m, 1H, Ment), 2.01-2.06 (m, 1H, Ment), 2.75 (bs, 1H, H-2''), 3.13 (dd, $J_{2',3'}$ = 9.6 Hz, $J_{2',1'}$ = 3.4 Hz, 1H, H-2'), 3.42-3.55 (m, 8H), 3.57 (dd, $J_{5,4}$ = 10.9 Hz, $J_{5,6}$ = 8.4 Hz, 1H, H-5), 3.60-3.69 (m, 4H), 3.65 (t, $J_{4''',3'''} = J_{4''',5'''}$ = 8.9 Hz, 1H, H-4'''), 3.79-3.87 (m, 3H), 3.95 (dd, $J_{4,5}$ = 10.9 Hz, $J_{4,3}$ = 7.3 Hz, 1H, H-4), 4.08 (dd, $J_{6,5}$ = 8.4 Hz, $J_{6,1}$ = 2.4 Hz, 1H, H-6), 4.12-4.18 (m, 2H), 4.21 (dd, $J_{2''',3'''}$ = 10.3 Hz, $J_{2''',1'''}$ = 8.3 Hz, 1H, H-2'''), 4.32 (dd, $J_{3''',2'''}$ = 10.3 Hz, $J_{3''',4'''}$ = 8.9 Hz, 1H, H-3'''), 4.36 (t, $J_{3,4} = J_{3,2}$ = 7.3 Hz, 1H, H-3), 4.39-4.52 (m, 6H), 4.53 (dd, $J_{2,3}$ = 6.9 Hz, $J_{2,1}$ = 4.0 Hz, 1H, H-2), 4.67 (dd, 1H, CH_2Ph), 4.87 (bs, 1H), 4.96 (dd, $J_{1,2}$ = 4.0 Hz, $J_{1,6}$ = 2.4 Hz, 1H, H-1), 5.13 (d, $J_{1''',2'''}$ = 8.3 Hz, 1H, H-1'''), 5.25 (d, $J_{1',2'}$ = 3.4 Hz, 1H, H-1'), 5.44 (s, 1H, H-7'''), 6.76-7.61 (m, 44H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 16.08, 19.31, 20.78, 21.92, 23.17, 23.60, 23.73, 23.90, 24.77, 25.06, 25.93, 26.97, 31.43, 34.08, 34.52, 36.16, 36.30, 36.68, 40.60, 47.00, 55.57, 62.68, 66.10, 68.73, 69.43, 70.44, 71.23, 72.09, 73.10, 73.25, 73.95, 74.66, 76.50, 76.70, 78.84, 79.28, 80.00, 82.91, 96.22, 98.07, 98.90, 101.24, 112.19, 113.49, 123.12, 126.08, 126.61, 126.77, 127.29, 127.51, 127.72, 127.91, 127.97, 128.10, 128.20, 128.26, 128.95, 129.69, 129.81, 131.54, 133.46, 133.62, 134.48, 136.07, 137.46, 137.75, 138.05, 138.59, 154.16. Anal. Calcd. for $C_{113}H_{130}N_4O_{23}Si$: C, 69.95; H, 6.75; N, 2.89. Found: C, 69.78; H, 6.85; N, 2.72.

***O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→6)-*O*-(2,4-di-*O*-benzyl-3-α-D-mannopyranosyl)-(1→4)-*O*-[6-*O*-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)]-2,3:4,5-di-*O*-cyclohexyliden-1-*O*-menthoxycarbonyl-*myo*-inositol (42).** 6 mL of a solution 0.92M of tetrabutylammonium fluoride buffered with acetic acid in THF, were added to 71 mg (0.036 mmol) of **41**. The reaction mixture was stirred for 10 days at 50°C, then cooled and quenched with water, diluted and extracted with CH_2Cl_2 and dried with Na_2SO_4. Silica-gel column chromatography (hexane-EtOAc, 3:1) afforded **42** in 88% yield. TLC: R_f(hexane-EtOAc, 3:1) = 0.23. M.p. = 103-105°C. $[\alpha]_D$ +37.866° (*c* 0.60, $CHCl_3$). ^{1}H NMR (300 MHz, C_6D_6) δ: 0.69-0.71 (m, 1H, Ment), 0.81 (d, 3H, CH_3Ment), 0.95 (d, 6H, CH_3Ment), 0.87-1.80 (m, 24H), 1.99-2.03 (m, 2H, Ment), 2.13 (d, $J_{3'',OH}$ = 9.5 Hz, 1H, OH), 2.15-2.27 (m, 2H, Ment), 3.17 (dd, $J_{2',3'}$ = 10.4 Hz, $J_{2',1'}$ = 3.5 Hz, 1H, H-2'), 3.49-3.53 (m, 2H), 3.62-3.65 (m, 1H),

3.67 (dd, $J_{2'',3''}$ = 3.3 Hz, $J_{2'',1''}$ = 1.5 Hz, 1H, H-2''), 3.72-3.89 (m, 4H), 4.18 (dd, $J_{3',2'}$ = 10.2 Hz, $J_{3',4'}$ = 9.0 Hz, 1H, H-3'), 3.96-4.48 (m, 13H), 4.58 (dd, $J_{6,1}$ = 2.9 Hz, 1H, H-6), 4.68 (dd, $J_{2,3}$ = 6.7 Hz, $J_{2,1}$ = 4.1 Hz, 1H, H-2), 4.56-4.91 (m, 9H), 5.33 (s, 1H, H-7'''), 5.40 (d, $J_{1'',2''}$ = 1.4 Hz, 1H, H-1''), 5.44 (dd, $J_{1,2}$ = 3.9 Hz, $J_{1,6}$ = 3.1 Hz, 1H, H-1), 5.50 (d, $J_{1''',2'''}$ = 8.1 Hz, 1H, H-1'''), 5.69 (d, $J_{1',2'}$ = 3.5 Hz, 1H, H-1'), 6.78-6.83 (m, 2H, ArH), 6.85-6.90 (m, 2H, ArH), 7.04-7.40 (m, 26H, ArH), 7.47-7.41 (m, 2H, ArH), 7.66-7.69 (m, 2H, ArH). ^{13}C NMR (50 MHz, C_6D_6) δ: 16.53, 20.86, 22.01, 23.57, 23.94, 24.10, 24.35, 25.14, 25.42, 26.48, 31.46, 34.23, 35.06, 36.67, 36.88, 37.08, 40.89, 47.50, 56.35, 63.21, 66.42, 68.57, 68.83, 69.84, 71.65, 71.81, 71.98, 72.06, 73.57, 73.83, 74.15, 74.87, 75.30, 76.32, 76.72, 77.04, 77.25, 77.43, 77.96, 79.20, 79.29, 80.45, 83.35, 97.12, 98.79, 99.26, 101.43, 112.15, 113.48, 118.92, 123.26, 126.65, 127.70, 128.98, 129.48, 129.66, 129.92, 132.16, 133.46, 138.32, 138.43, 138.62, 138.75, 139.30, 139.37, 154.90, 167.91. Anal. Calcd. for $C_{97}H_{112}N_4O_{23}$: C, 68.46; H, 6.63; N, 3.29. Found: C, 68.11; H, 6.55; N, 3.33.

***O*-(6-*O*-acetyl-2-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranosyl) - (1→6)-*O*-(2-*O* - benzyl- 3,4-*O* -isopropyliden - α- D -galactopyranosyl)-(1→3)-*O*-[*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→6)-]-*O*-(2,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-*O*-[6-*O*-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)]-2,3:4,5-di-*O*-cyclohexyliden-1-*O*-menthoxycarbonyl-*myo*-inositol (43).** A solution of 94 mg (0.119 mmol) of **40β**, 45 mg (0.026 mmol) of **42** and activated powdered 4Å molecular sieves in 0.6 mL of ethyl ether was stirred for 90 min. at room temperature. At this moment, 37 μL (0.004 mmol) of a solution of trimethylsilyl triflate in ethyl ether (0.108M) were added. The reaction mixture was stirred for 45 min., quenched with triethyl amine, diluted with CH_2Cl_2, filtrated through celite and evaporated *in vacuo*. Silica-gel column chromatographys (2 x cyclohexane-Et_2O, 5:2) afforded **43** (α/β = 6.5:1) in 83% yield. TLC: R_f(hexane-EtOAc, 3:1) = 0.26. M.p.: 93-96°C. $[\alpha]_D$ +54.112° (*c* 0.880, acetone). ^{1}H NMR (500 MHz, C_6D_6, 70°C) δ: 0.62-0.71 (m, 1H, Ment), 0.76 (d, 3H, CH_3Ment), 0.88 (d, 3H, CH_3Ment), 0.89 (d, 3H, CH_3Ment), 1.20 (s, 3H, ^{i}Pr), 1.29 (s, 3H, ^{i}Pr), 1.33 (s, 6H, ^{i}Pr), 0.84-1.78 (m, 24H), 1.74 (s, 3H, Ac), 1.89-1.93 (m, 2H, Ment), 2.12-2.18 (m, 2H, Ment), 3.35 (dd, $J_{2,3}$ = 10.4 Hz, $J_{2,1}$ = 3.7 Hz, 1H, H-2b), 3.44-3.46 (m, 1H), 3.49 (t, *J* = 9.9 Hz, 1H, H-d), 3.58-3.61 (m, 2H, H-2e, H-d), 3.64 (dd, $J_{2,1}$ = 3.4 Hz, $J_{2,3}$ = 7.6 Hz, 1H, H-2f), 3.67-3.74 (m, 2H, H-a), 3.96 (t, *J* = 9.2 Hz, 1H), 3.99-4.01 (m, 2H, H-e), 4.06-4.20 (m, 9H, H-f, H-d, H-2c, H-a), 4.23 (t, *J* = 9.6 Hz, 1H, H-b), 4.30-4.69 (m, 23H), 4.71 (dt, 1H, Ment), 4.78-5.00 (m, 4H, CH_2Ph), 4.94 (d, *J* = 3.1 Hz, 1H, H-1f), 5.13 (d, *J* = 3.0 Hz, 1H, H-e), 5.3 (s, 1H, H-7d), 5.33 (t, *J* = 3.5 Hz, 1H, H-2a), 5.42 (m, 1H, H-1d), 5.58 (d, $J_{1,2}$ = 3.7 Hz, 1H, H-1b), 5.62 (d, $J_{1,2}$ = 1.8

Hz, 1H, H-1c), 6.76-7.57 (m, 44H, ArH). ^{13}C NMR (75 MHz, C_6D_6, 50°C) δ: 16.67, 20.52, 20.84, 21.99, 23.79, 24.14, 24.24, 24.38, 25.28, 25.50, 26.45, 26.65, 26.99, 28.19, 30.12, 31.56, 34.38, 35.14, 36.75, 37.03, 37.23, 41.01, 47.63, 56.47, 63.15, 64.06, 66.51, 66.56, 67.35, 67.64, 68.93, 70.14, 71.34, 71.79, 72.63, 72.79, 73.52, 73.66, 73.89, 74.01, 74.24, 74.74, 74.93, 75.61, 76.22, 76.91, 77.06, 77.23, 77.48, 78.02, 78.16, 78.81, 79.31, 80.97, 83.42, 97.56 (C1N3), 97.94 (C1Man, C1Gal'), 99.36 (C1NPht), 99.43 (C1Gal), 101.57 (Bencylidene), 108.94 (4°, iPr), 109.56 (4°, iPr), 112.16 (4°, CHex), 113.42 (4°, CHex), 123.36, 126.69, 127.03, 127.20, 129.28, 129.36, 132.33, 133.51, 138.75, 138.87, 138.94, 139.03, 139.50, 139.65, 154.88 (carbonate), 167,97 (NPht), 169.99 (NPht).

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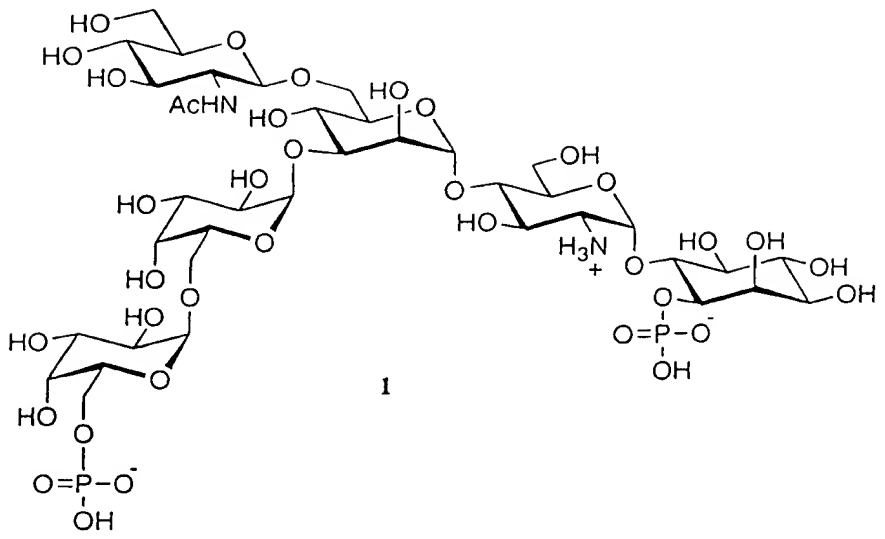
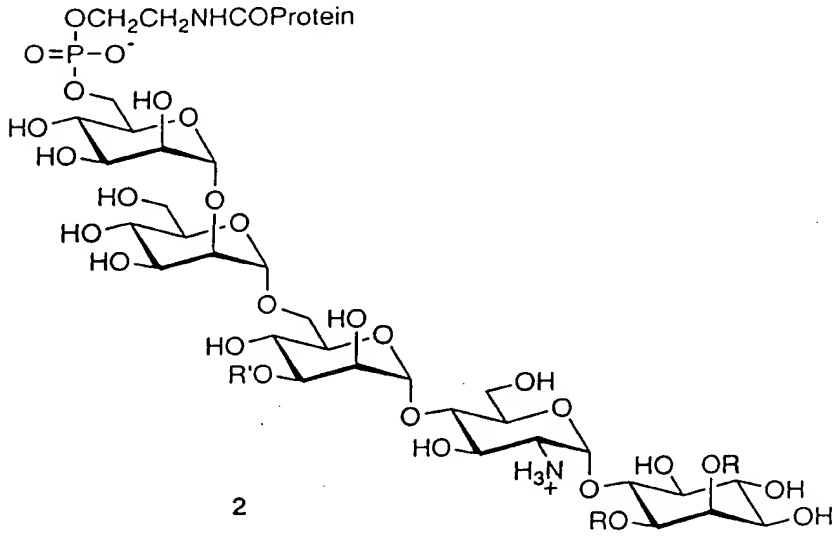


1



2

FIGURE 1

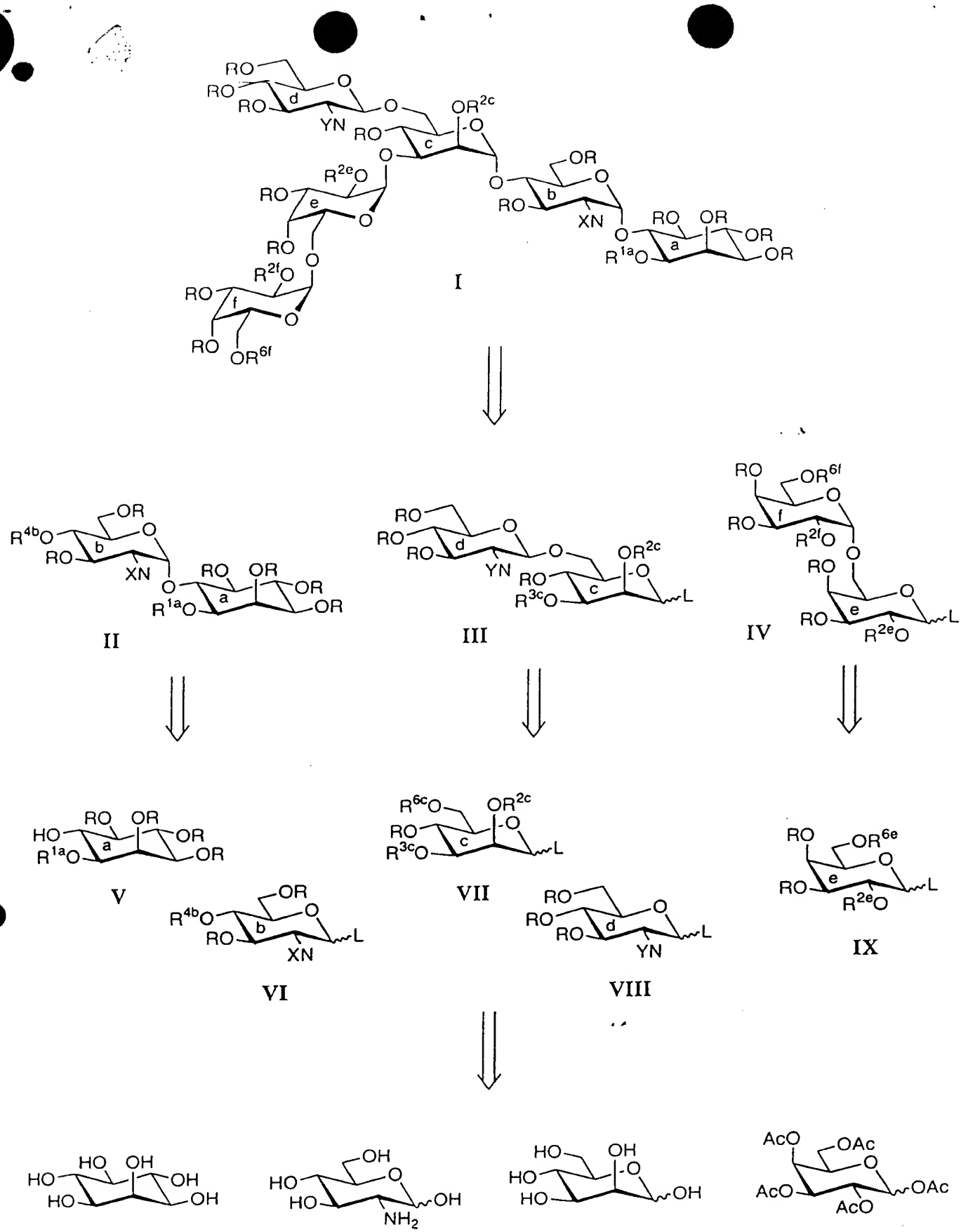
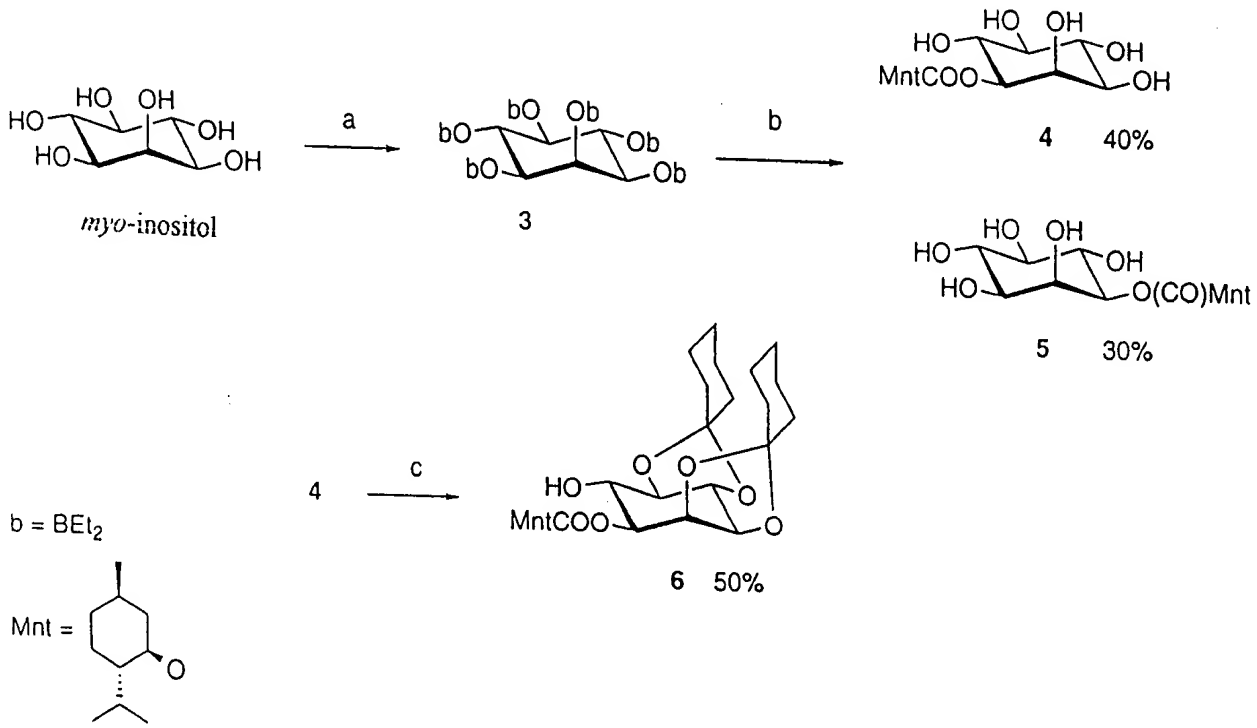
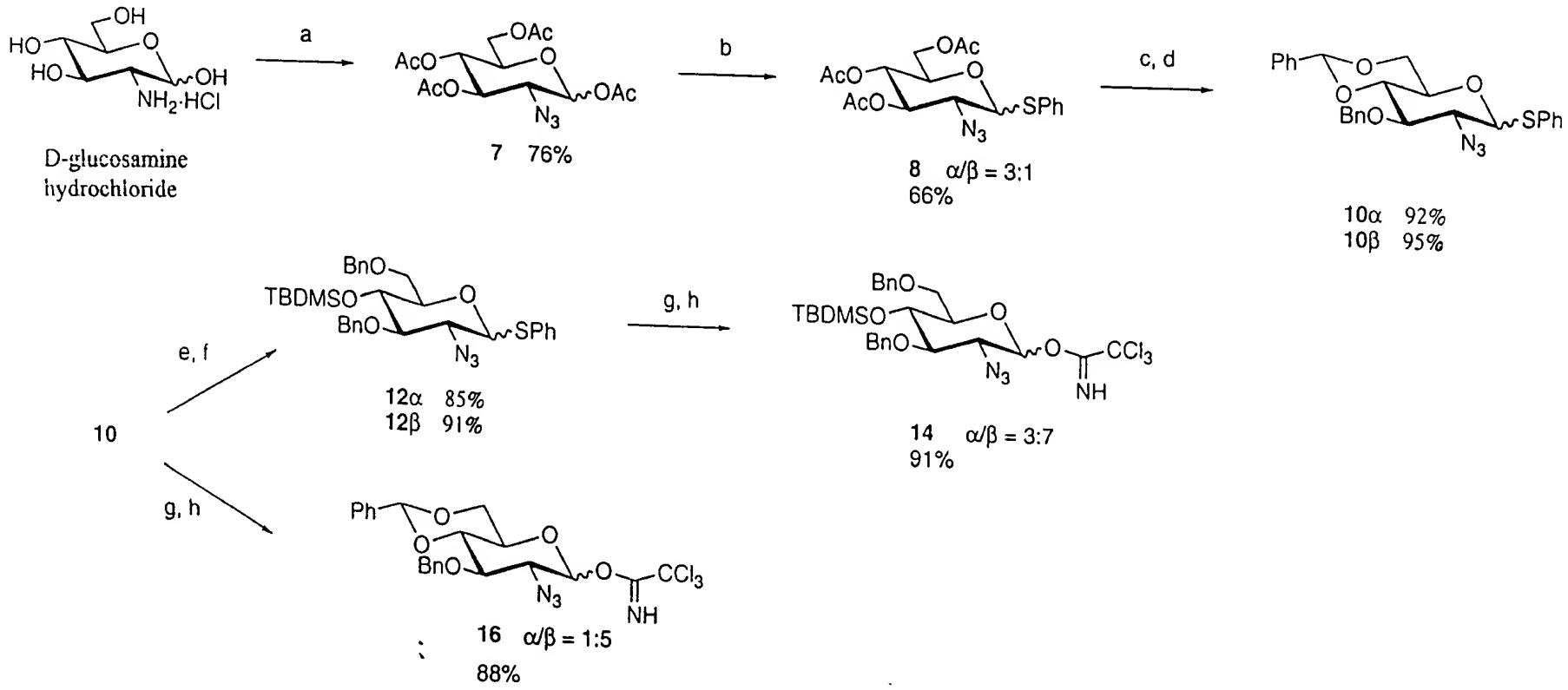


FIGURE 2



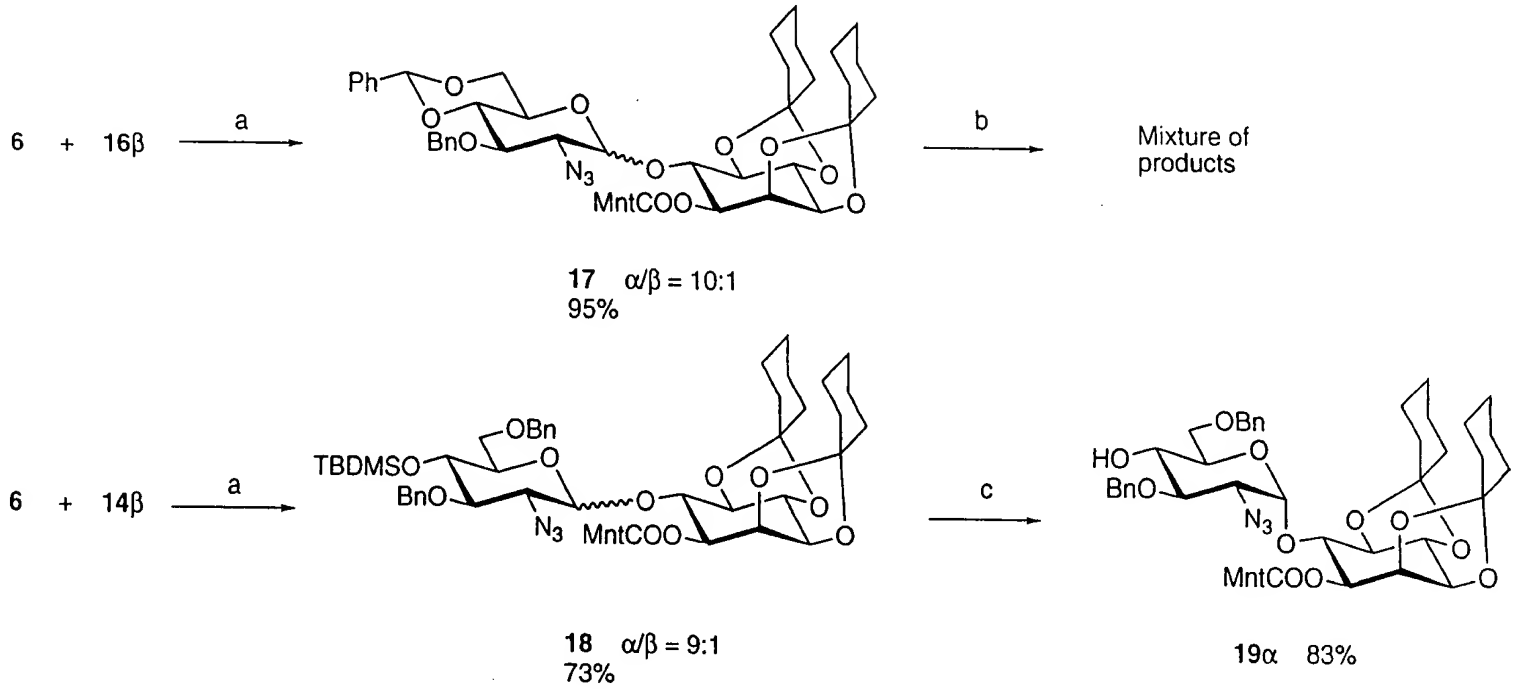
a) $Et_3B/^tBuCO_2BEt_2$, hex, TA; b) i,$Bu_2Sn(acac)_2$, tol,RT; ii, (-)-MntCOCl, NMI, -30 °C → RT; iii, MeOH;
c) 1-ethoxycyclohexene, *p*-TsOH,RT, cyclohexanone

FIGURE 3



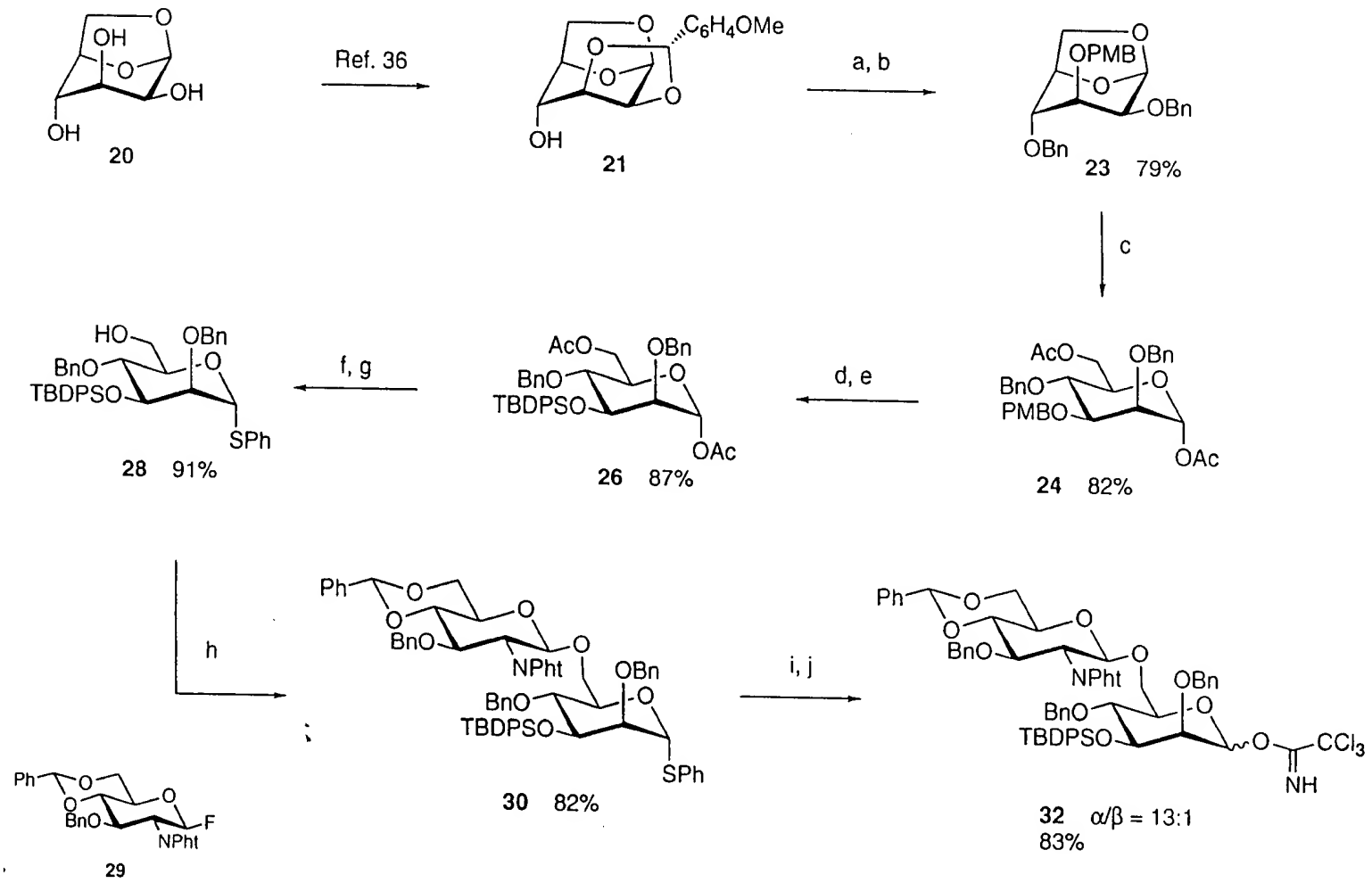
a) i, NaOMe, MeOH; ii, TfN_3, DMAP, CH_2Cl_2; iii, Ac_2O, py; b) $BF_3{\cdot}Et_2O$, PhSH, CH_2Cl_2, RT; c) i, NaOMe, MeOH; ii, benzaldehyde dimethylacetal, *p*TsOH, CH_3CN, RT; d) BnBr, NaH, DMF, RT; e) i, $NaCNBH_3$, THF, RT; ii, HCl/Et_2O; f) TBDMSOTf, col, CH_2Cl_2, 0 °C, g) NBS, -15 °C, acetone/H_2O; h) CCl_3CN, K_2CO_3, CH_2Cl_2, RT

FIGURE 4



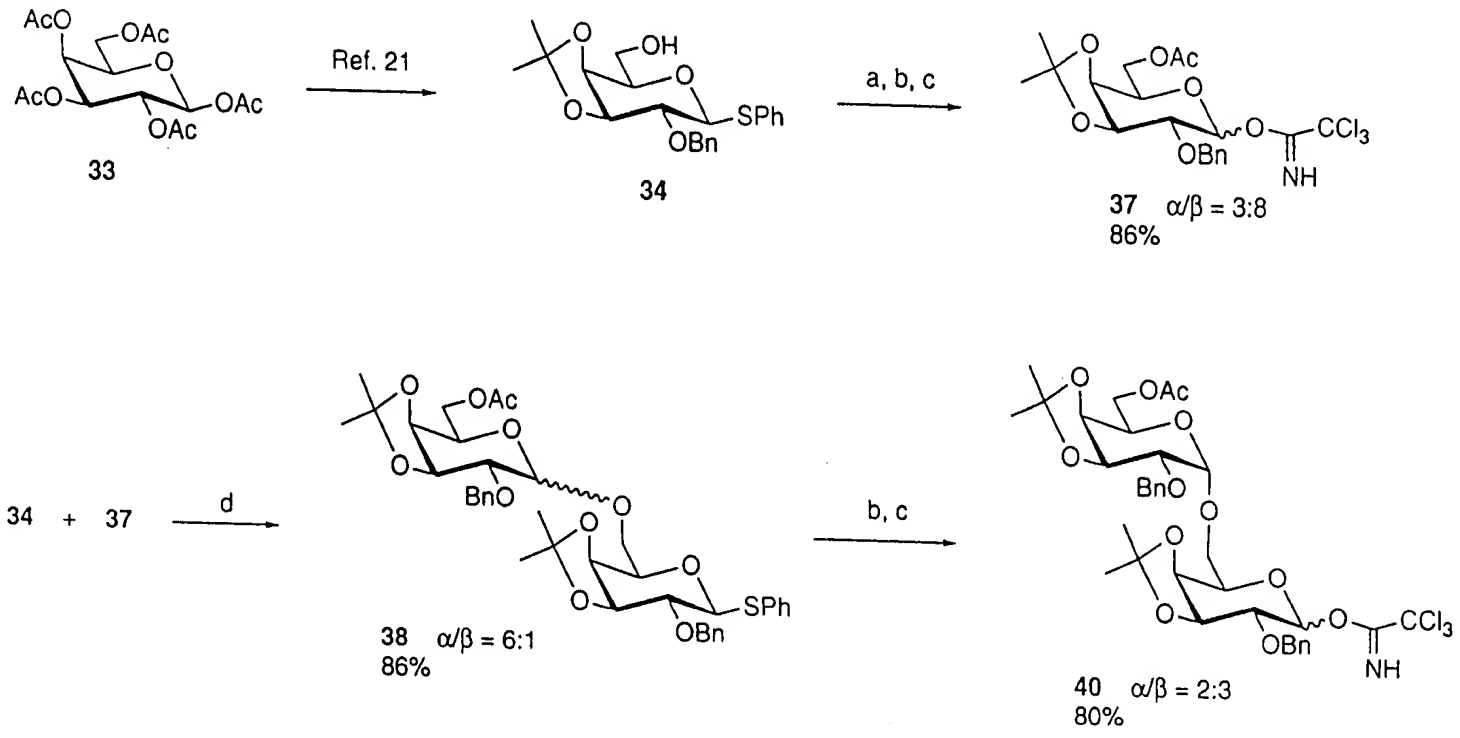
a) TMSOTf, RT, Et_2O, 4 Å MS; b) i, $NaCNBH_3$,THF, RT; ii, HCl/Et_2O; c) TBAF, THF, RT

FIGURE 5



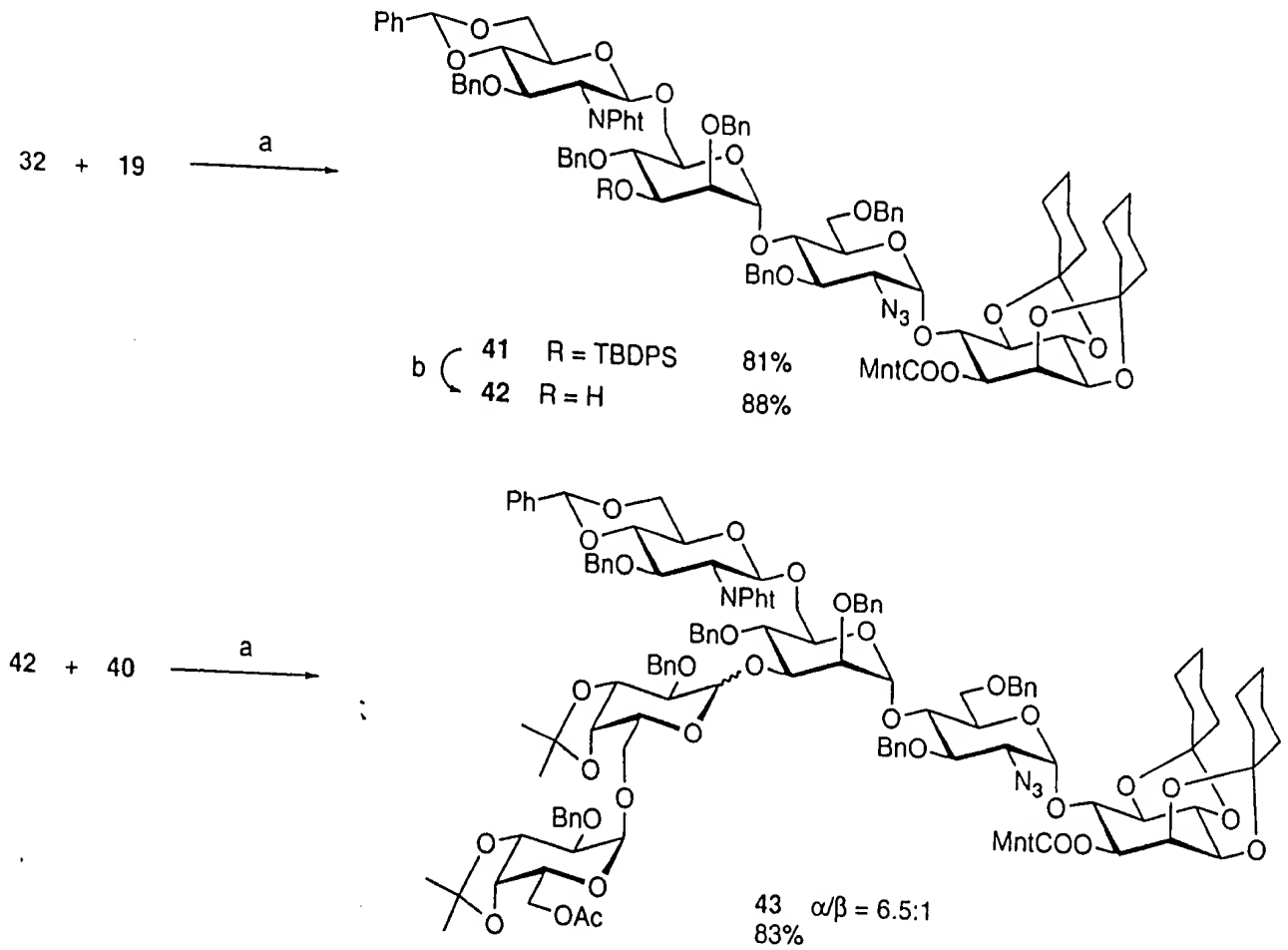
a) DIBALH, CH_2Cl_2, 0 °C → RT; b) NaH, BnBr, DMF, RT; c) TMSOTf, Ac_2O, d) TFA 4%, CH_2Cl_2, RT; e) TBDPSCl, DMF, DMAP, Im, RT; f) $BF_3{\cdot}Et_2O$, RT, PhSH, CH_2Cl_2; g) NaOMe/MeOH; h) i, AgOTf, Cp_2ZrCl_2, CH_2Cl_2, -40 °C, 4 Å MS, ii, **29**; i) NBS, -15 °C, acetone/H_2O; j) CCl_3CN, K_2CO_3, CH_2Cl_2, RT

FIGURE 6



a) Ac_2O, py, DMAP; b) NBS, -15 °C, acetona/H_2O; c) K_2CO_3, CCl_3CN, CH_2Cl_2, RT;
d) TMSOTf, Et_2O, RT, 4 Å MS

FIGURE 7



a) TMSOTf, RT, Et_2O, 4 Å MS; b) TBAF, AcOH, THF, 50 °C

FIGURE 8

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